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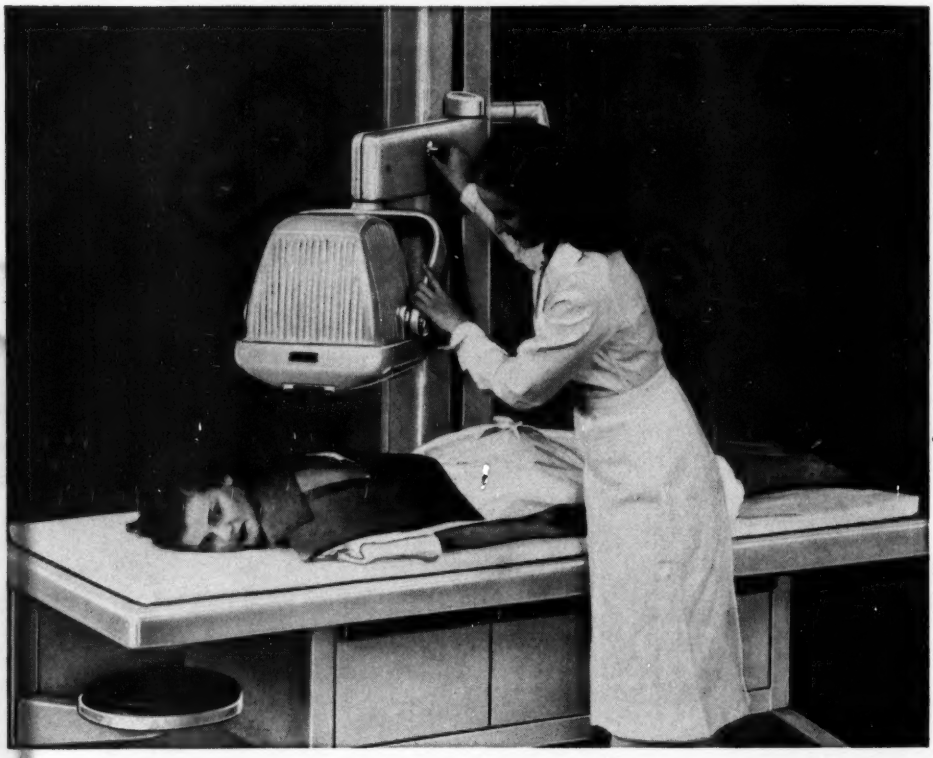

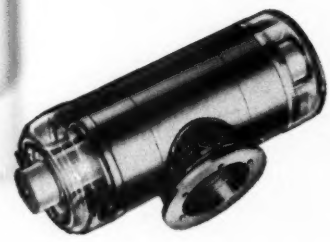

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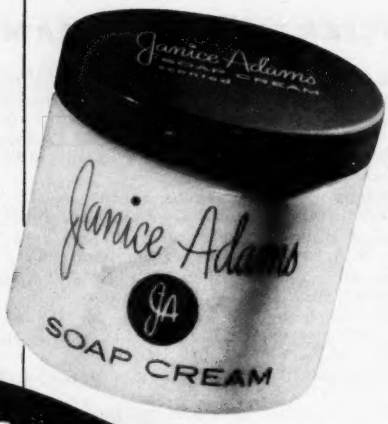

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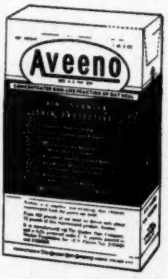

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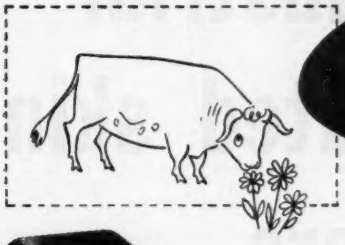

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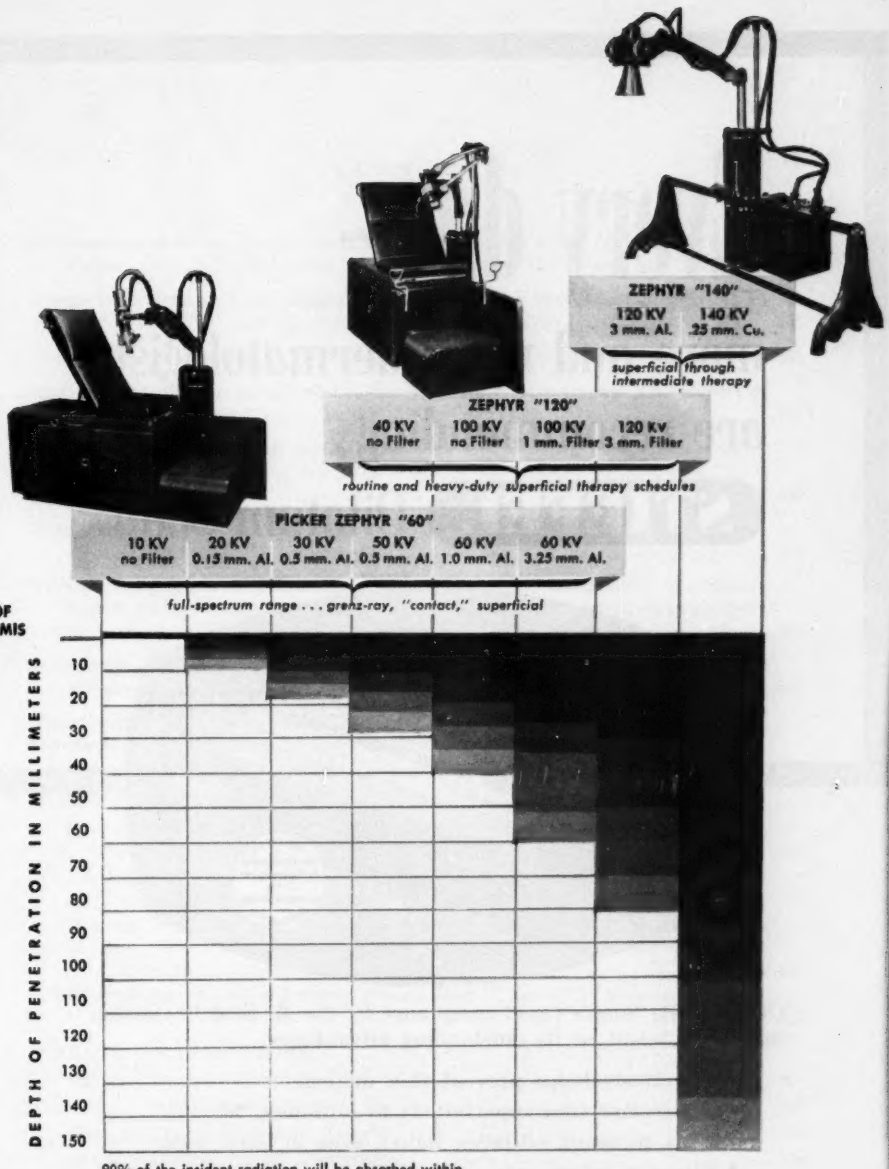

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MANAGEMENT OF ATOPIC DERMATITIS IN CHILDREN CONTROL OF THE MATERNAL REJECTION FACTOR

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SIXTEEN years ago, in concluding an excellent presentation on atopic eczema in childhood, Hill [1] stated:

> To talk about eczema is easy and always pleasant; to cure the patient is quite another matter, and in spite of allergens, reagins, skin tests, elimination diets, and so on, the actual practical treatment is not entirely satisfactory, whether by dermatologist, allergist or pediatrician, or by all combined.

Most dermatologists today would agree that this still constitutes a reasonable assessment of the status of the therapeutic effectiveness of existing measures to deal with atopic dermatitis.

About the time this opinion was being expressed, however, a few voices were being raised to introduce a new viewpoint on the pathogenesis of atopic dermatitis. Sack,[2] Stokes,[3] Blaisdell [4] and Becker [5] drew attention to associated neurogenic and psychogenic factors, to emotional states and to neurocirculatory instability in prurigo, neurogenous dermatitis and eczema. These were the early stirrings of a new etiological concept of atopic dermatitis—a concept which, since then, has kept pace with the rapid permeation of the entire field of scientific medicine with the leaven of "humanism," a concept which has increasingly recognized the part man's inherent emotional reaction to life as he meets it bears to his happiness and to his woe, to his health and to his illness.

Having belatedly confirmed the truth of Hill's wise opinion regarding the inadequacy of existing methods of treating atopic dermatitis in children, I began to explore the field of the personality and human relationships of children with

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Read at the Seventieth Annual Meeting of the American Dermatological Association, Inc., Jasper National Park, Alta., Canada, June 20, 1950.

1. Hill, L. W.: Chronic Atopic Eczema (Neurodermatitis) in Childhood, J. A. M. A. **103**:1430-1434 (Nov. 10) 1934.

2. Sack, W. T., cited by Dunbar, H. F.: Emotions and Bodily Changes: A Survey of Literature on Psychosomatic Interrelationships, 1910-1933, published for the Josiah Macy, Jr. Foundation, New York, Columbia University Press, 1935, p. 388.

3. Stokes, J. H.: The Complex of Eczema: A Diagnostic and Etiologic Analysis, J. A. M. A. **98**:1127-1133 (April 2) 1932.

4. Blaisdell, J. H.: Mental Allergy, Arch. Dermat. & Syph. **25**:205-212 (Feb.) 1932.

5. Becker, S. W.: Dermatoses Associated with Neurocirculatory Instability, Arch. Dermat. & Syph. **25**:655-682 (April) 1932.

"flexural eczema" along the lines originally defined by Rogerson [6] and later extended with lucidity by Wittkower.[7] It became increasingly apparent, as I delved into this realm, that these children conformed to a specific personality pattern and that in almost all instances the child appeared to be faced with rejection by the one human being who was closest and on whom he was most dependent, the mother. On these observations a plan of therapy was evolved which attempted, wherever possible, by sympathetic, tactful counseling of the mother, to correct the factor of maternal rejection.

In presenting this study in the management of atopic dermatitis, I feel like one who, suffering as the result of psychic "scotoma" [2] from Sack's occupational blindness of dermatologists, joins the company of those groping around the elephantine colossus of atopic dermatitis and attempting to determine from various vantage points, by a sensation less acute than the visual one, the extent of this wondrous

Fig. 1.—"Seeing" the elephant (illustration by Lois Lenski for John Godfrey Saxe's "The Blind Men and the Elephant," in Hutchinson, V. S.: Fireside Poems, New York, Minton, Balch & Company, 1930; copyright, 1930, by Minton, Balch & Company courtesy of J. P. Putnam's Sons).

beast, much as did the blind men in John Godfrey Saxe's famous "Hindoo fable," which relates how

> It was six men of Indostan
> To learning much inclined
> Who went to see the Elephant
> (Though all of them were blind).
> That each by observation
> Might satisfy his mind.

Each in his blindness "saw" the elephant differently—one as a wall, another as a spear, a third as a snake, and so on—as a tree, a fan and a rope. So the situation would appear to have been with wondrous, enigmatic atopic dermatitis in the past 25 years. Various authorities from various vantage points have viewed this dermatological "elephant" and gained various impressions of it—a diathesis, vagotonia, atopic allergy, neurocirculatory instability, protoplasmic irritability, dysfunction of

6. Rogerson, C. H.: The Psychological Factors in Asthma-Prurigo, Quart. J. Med. **6**: 367-394 (Oct.) 1937.

7. Wittkower, E.: Psychological Aspects of Dermatology, in MacKenna, R. M. B.: Modern Trends in Dermatology, London, Butterworth & Co., Ltd., 1948, chap. 2, pp. 237-252.

autonomic chemical mediation, histamine effect, result of acetylcholine liberation, an inherent personality problem and a psychogenic and emotional disturbance, among others. This presentation throws the spotlight of interest on only one aspect of a complex problem, with the full realization that, as the point was so aptly put by Hill,[1] "The understanding of this disease is constantly increasing, but there are many things unexplained, and the kernel of it has by no means as yet been explained."

ETIOLOGICAL CONCEPTS

After Besnier's recognition of prurigo in 1892 and its close relationship to asthma and hay fever, there followed a barren period of investigative indifference which lasted nearly 30 years. Then, in the 1920's, from three independent fields of medical thought and study, there appeared a beginning interest in the pathogenesis of the asthma-eczema-hay fever syndrome, and arising therefrom came certain therapeutic proposals.

The first field of research that had a bearing on the problem was represented by that brilliant sequence of fundamental biochemical, physiological and clinical studies on the chemical mediation of nerve impulses, histamine metabolism and neurovascular dynamics, with its illustrious heritage of workers, including Elliott, Dale, Lewis, Cannon and Loewi,[8] this line of investigation presently being pursued in the dermatological field by Rothman and his group.[9] The second field of study was that dealing with altered tissue reaction—the allergic state. Experiments therein have produced the most definitive objective evidence of consistent altered tissue reaction in the asthma-eczema-hay fever triad. Coca[10] and Sulzberger[11] demonstrated by biologic tests the inseparable association of atopic reagins in Besnier's pruriginous diathesis. Recognition of this fundamental contribution is seen in the common acceptance of the term "atopic dermatitis" for the clinical condition under consideration. Reference has already been made to the third field—that field occupying the attention of authorities who were doing the pioneer work in the neurogenic and psychogenic aspects of atopic dermatitis. The original workers have been joined in this field by an increasing number of investigators,[12] whose studies have done much to define more clearly the associated emotional factors.

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8. Butt, H. R.: Recent Advances in Knowledge Concerning Chemical Mediation of Nerve Impulses, Proc. Staff Meet., Mayo Clin. **11**:321-326 (May 20) 1936.

9. Rothman, S.: The Role of the Autonomic Nervous System in Cutaneous Disorders, Psychosom. Med. **7**:90-96 (March) 1945.

10. Coca, A. F.; Walzer, M., and Thommen, A. A.: Asthma and Hay Fever in Theory and Practice, Springfield, Ill., Charles C Thomas, Publisher, 1931.

11. Sulzberger, M. B.: Dermatologic Allergy, Springfield, Ill., Charles C Thomas, Publisher, 1940, pp. 129-178.

12. Stokes, J. H., and Beerman, H.: Psychosomatic Correlations in Allergic Conditions, Psychosom. Med. **2**:438-458 (Oct.) 1940. Greenhill, M. H., and Finsinger, J. E.: Neurotic Symptoms and Emotional Factors in Atopic Dermatitis, Arch. Dermat. & Syph. **46**:187-200 (Aug.) 1943. Lynch, F. W.; Hinckley, R. G., and Cowan, D. W.: Psychosomatic Studies in Dermatology: Psychobiologic Studies of Patients with Atopic Eczema (Disseminated Neurodermatitis), ibid. **51**:251-260 (April) 1945. Woodhead, B.: Psychological Aspect of Allergic Skin Reactions in Childhood, Arch. Dis. Childhood **21**:98-104 (June) 1946. Cormia, F. E.: Psychosomatic Factors in Dermatoses: A Critical Analysis of Diagnostic Methods of Approach, Arch. Dermat. & Syph. **55**:601-620 (May) 1947. Sulzberger, M. B., and Zaidens, S.: Psychogenic Factors in Dermatologic Disorders, M. Clin. North America **32**:675, 681-683 (May) 1948.

Rogerson [6] emphasized the role of the overanxious protecting parent on the sensitive atopic child and clearly demonstrated the influence of parental behavior in precipitating and aggravating clinical forms of atopy. Wittkower's [7] studies on personality types, the properties of character and the emotional reactions of individuals have assisted in classifying the atopic person as a compulsive or obsessional type. The recent investigations of Walsh and Kierland [13] confirm that there is a characteristic emotional pattern of adults with generalized neurodermatitis and underline the features of narcissism, strong superego and the need for affection.

Increasing study on the interpersonal relationships in the home has tended to demonstrate that the behavior of the mother toward the child with clinical manifestations of atopy may have considerable etiological significance. Miller and Baruch [14] in a study of 63 children with asthma, hay fever, eczema and urticaria found that "maternal rejection is not only an almost universal experience in the lives of allergic children, but they differ in this regard from other groups of problem children." French and Alexander [15] and Mohr and co-workers [16] provided earlier evidence of maternal rejection in children with asthma. Figge,[17] Newell,[18] and Levy [19] have recorded the results of their respective careful investigations on the etiology and psychodynamics of maternal rejection and its effect on the child's behavior.

Referring again to the three fields of thought and investigative effort—those dealing with the autonomic-chemical-mediative, the atopic and the psychogenic aspects of the problem—it would appear that each, from an apparently opposite and divergent point, is in fact approaching the others, and it would seem only reasonable that ultimately they will reach that common ground where the intangible factors of life expressing themselves in tangible clinical manifestations will be revealed by our finer objective scientific studies to be the workings of delicate, precise biochemical and biophysical processes. Till that common ground is reached it is essential that research be pressed from all points, however divergent and opposite they may appear.

CLINICAL MATERIAL

The clinical material in this study consisted of 53 children (22 boys and 31 girls) between the ages of 13 months and 12 years with chronic "flexural eczema." In all children the antecubical and popliteal areas were involved in a chronic licheni-

13. Walsh, M. N., and Kierland, R. R.: Psychotherapy in the Treatment of Neurodermatitis, Proc. Staff Meet., Mayo Clin. **22**:578-584 (Dec. 10) 1947.

14. Miller, H., and Baruch, D. W.: Psychosomatic Studies of Children with Allergic Manifestations: I. Maternal Rejection; A Study of 63 Cases, Psychosom. Med. **10**:274-278 (Sept.-Oct.) 1948.

15. French, T. M., and others: Psychogenic Factors in Bronchial Asthma, Psychosomatic Medicine Monographs IV, Washington, D. C., National Research Council, 1941, vol. 2, no. 1, pp. 70, 71.

16. Mohr, G.; Gerard, M., and Rosa, H., in French, Alexander and others,[15] p. 81.

17. Figge, M.: Some Factors in the Etiology of Maternal Rejection, Smith College Studies in Social Work, Northampton, Mass., Smith College, Sept.-June, 1931-1932, vol. 2, pp. 237-260.

18. (*a*) Newell, H. W.: The Psycho-Dynamics of Maternal Rejection, Am. J. Orthopsychiat. **4**:387-401 (July) 1934; (*b*) A Further Study of Maternal Rejection, ibid. **6**:576-589 (Oct.) 1936.

19. Levy, D. M.: Maternal Overprotection, Psychiatry **2**:99-109, 1939.

fied, excoriated dermatitis, and in 46 of them the process also affected the face, neck and wrists. In all the characteristic paroxysmal pruritus, worse during the early hours after going to sleep and aggravated by any "overheating" influence during the day, was present. In 46 instances the atopic dermatitis first became evident during the 12 months following birth; 27 of these patients manifested symptoms between the second and fourth month. At the time of examination and institution of therapy the dermatitis had been present for periods varying from six months to 11 years. Thirty of the children had had symptoms for 12 to 30 months. The usual tendency to winter exacerbation was experienced by most children. In two the condition was distinctly worse in summer. Nineteen subjects had associated clinical forms of atopy, of which vasomotor rhinitis was commonest. Familial atopy was present in 39 instances.

For purposes of comparative study the clinical material was divided into two groups. In the first group, comprised of 33 children, the therapeutic emphasis was on management of the maternal rejection factor. Wittkower's criteria[7] for assessing personality types were applied to the children within the limitations imposed by the age of the patients, and unusual features of behavior were noted. In this group a study was also made of the maternal rejection factor with the use of Newell's criteria.[18b] The second, or control, group consisted of 20 children who were treated without any direct or indirect approach with regard to personality type, emotional reactions or the interpersonal relationships of the child and the mother. Therapeutic effort was directed principally toward the elimination of potential dietary and air-borne allergens and to the use of coal tar topical applications. Planned elimination diets and the use of a food diary to indicate any discernible cause-effect relationships of food items and exacerbations were undertaken. The application of 1 per cent coal tar ointment with the occasional addition of ammoniated mercury was the usual local treatment. Roentgen rays were not applied. Phenobarbital sedation was given in a few instances for only a short period.

Of the 33 children in the first group 26 clearly came within the compulsive personality group as defined by Wittkower. Of these, 25 were aggressive with particular evidence of wilfulness, resistiveness and hostility toward the mother. One child was abnormally submissive in behavior. The children tended to be fear ridden to a varying degree, a prominent fear among them being that of darkness and going to sleep, which in 16 instances required that the bedroom light be kept burning and the door be left open. Thumb sucking, lip sucking, nail biting and thread picking appeared to be present among them to a greater extent than among other children.

Applying Newell's criteria for maternal rejection to the mothers of the 33 children, this conscious or unconscious behavior trait was found to be present in 31 cases. In the remaining two instances the mothers demonstrated attitudes toward their children which were suggestive of rejection. The mother of the submissive child exhibited, as might be expected, a pronounced oversolicitous type of maternal rejection. With the use of the duration of breast feeding as an index of maternal rejection, as suggested by Levy,[19] it was noted that 22 of the 33 children either were not breast fed or were breast fed for less than one month. Four children were breast fed for six months or longer.

The common relationship between the mother and child may be concisely pictured as a rather continuous smoldering and frequently open "battle of wills" between a tired, somewhat irritable, overwrought, coffee-drinking, poorly sleeping mother and a restless, resistive, strong-willed, highly intelligent, flexure-scratching child.

MANAGEMENT OF MATERNAL REJECTION

Treatment of the group of 33 children with atopic dermatitis in whom the compulsive personality was prominent and in whose mothers rejection was usual consisted in a minimum of bland topical therapy and a maximum of emphasis on control of the attitude of maternal rejection and the factors contributing to this attitude.

The children were examined and their treatment outlined, and thereafter they were seen infrequently. No effort was made to control potential allergens through dietary or environmental manipulation. The skin was sponged once daily with warm water and a minimum of standard white soap used as needed on normal skin only. No sedatives were given. Topical therapy was restricted to the application of calamine liniment or lotion, zinc oxide ointment and, where secondary infection occurred, 2 per cent ammoniated mercury cream. Neither coal tar preparations nor roentgen rays were given.

After the institution of this simple regimen for the child the mother returned alone for a long, leisurely visit, during which the discussion was based on consideration of the basic emotional needs of a child, the effect on the child of withdrawal of satisfaction of these needs and the means of meeting these needs adequately. During this discussion an opportunity was provided of assessing the mother's and the child's emotional reactions and behavior pattern and thereby introducing specific advice concerning the correction of the apparent causal or contributory personality or environmental factors. The following comments served as an outline for the instruction and counseling given to the mother:

1. A mother's love, tender in quality and expressed by acts of love toward the child, satisfies the basic emotional need of every child and is particularly essential to the atopic child. This maternal love commences at the birth of the child and is expressed during the early months of his life in the tender intimacy of breast feeding. As the child grows this expression of affection is replaced by frequent daily acts of love toward the child, such as the enfolding arms, the caress and soft words. The mother's love is also expressed indirectly by her qualities of patience, understanding and forgiveness in her daily interpersonal relationships with the child.

2. The withdrawal of tender, expressed maternal affection from the atopic child is associated with anxiety or distress, which exhibits itself in the form of the characteristic pruritus of atopic dermatitis and as resistive, wilful hostility toward the mother. The child's nocturnal pruritic distress and hostile behavior engender anxiousness on the mother's part, which aggravates the maternal rejection, thereby setting up a vicious interpersonal emotion-behavior cycle between the mother and child, with consequent perpetuation of the atopic dermatitis.

3. The capacity for providing maternal love varies. The mother of the atopic child does not appear to have the ability to express affection spontaneously to any

great degree. It is essential for her, therefore, to cultivate the behavior of affection toward her child. She can accomplish this purpose by the following means:

(*a*) By being in good health and well rested. Hours of sleep should be continuous and adequate, the father doing any necessary night vigil. The "jet propellors"—tea, coffee and colas—should be restricted and mild sedation given.

(*b*) By enjoying a happy partnership with the father in an "even" home. Emotional explosions and scenes between marital partners, particularly before the child, are disastrous. Separation and divorce produce and aggravate maternal rejection.

(*c*) By expressing affection for the child frequently each day by the enfolding arms, the caress and tender words.

(*d*) By spending at least five tender minutes at the child's bedside each night. Doing so provides the best sedative an atopic child can be given before being cut off from the mother by darkness, uncontrollable dreams (frequently fearful) and the nocturnal distress of pruritus.

(*e*) By avoiding unreasonable, harsh discipline and following all verbal or corporal disciplinary action promptly within a few minutes with maternal forgiveness expressed by a reasonable explanation for the disciplinary action and by the enfolding arms, the caress and the tender word.

(*f*) By avoiding the use of frustrating, restrictive commands, threats and expletives, such as "No, don't do that!" "Stop it!" "Leave it alone!" "Get out of my way!" and "You make me sick!", which are frequently showered daily on the atopic child by the tired, irritable mother.

(*g*) By deftly avoiding any "clash of wills" or "joining battle" on any "issue" raised by the resistive, hostile atopic child, whether it be "eating peas," "wearing that blue dress" or "not touching that piece of Dresden," for example.

After this initial detailed discussion the mother and child were seen at increasingly infrequent intervals and on such occasions mainly for the purpose of counseling, not for the dispensing of a "new" ointment. In certain instances it was essential to arrange a visit to include the father.

RESULTS OF TREATMENT

In studying the effect of therapy on the 53 children with atopic dermatitis an observation period of 24 months after institution of treatment was selected for assessment. It was considered that this period made allowance for any false impression based on temporary seasonal improvement and was sufficiently long for one to gain a reasonable idea of any tendency to recurrence.

Response to treatment was divided into three categories: (1) persisting complete freedom from dermatitis, (2) clearly defined continuing improvement and (3) an essentially unchanged clinical course. The data on therapeutic response are shown in the accompanying table. At the end of a 24 month observation period 15 (45 per cent) children of the group of 33 in which emphasis had been placed upon maternal rejection were symptom free, whereas in the control group two out of 20 (10 per cent) had clearing. The comparative difference is enhanced when an analysis is made of the time interval between institution of therapy and complete freedom from symptoms. This is shown in figure 2. The 15 children in the "maternal

rejection" group who became symptom free did so in the seven months after starting treatment, 11 of them having clearing in three months. In the control group the two who became symptom free did not have clearing until the fifteenth and eighteenth month, respectively.

Therapeutic Response of Fifty-Three Children with Atopic Dermatitis Followed for Twenty-Four Months

Type of Therapy	No. Free from Dermatitis	No. with Improvement in Dermatitis	No. with Dermatitis Unchanged	Total
Management of maternal rejection	15 (45%)	15	3	33
"Control"	2 (10.0%)	14	4	20

Of the three children in the group in which maternal rejection was emphasized who were unimproved after 24 months, two lived in disturbed homes with irreconcilable tension between the parents and in the third instance the mother was very

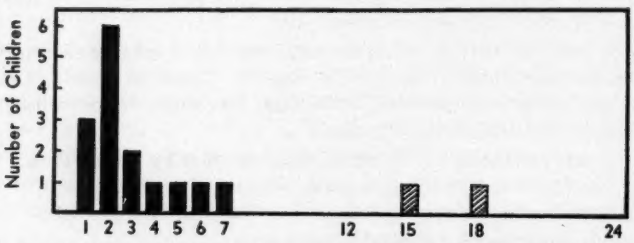

Fig. 2.—Data on a 24 month observation of 53 children with atopic dermatitis showing the time interval after therapy before 17 children became and remained symptom free. The solid blocks indicate children in the group managed on the basis of maternal rejection; the hatched portions, those managed on "control" therapy.

hostile to the idea that she might unwittingly be playing a role in the child's distress and insisted that the child was allergic to foods, though she couldn't specify any food items nor could she help the child's dermatitis by manipulating the diet. Of the 15 children who were improved, six lived in turbulent home environments with continuing parental emotional instability and friction.

In the control group only one mother felt that food had any bearing on the dermatitis. She named celery, carrots and spinach as specific exacerbators of the condition. In no other instance did food appear to play any clearly discernible part in causing or aggravating the dermatitis, nor was there any clearcut evidence that air-borne allergens played an etiological role, with the exception that winter aggravation in many children might be interpreted as the result of increased exposure to house dust.

COMMENT

In discussing the results of this study I wish at the outset to make it clear that this investigation involves only the "feeling" of a portion of that wondrous elephant, atopic dermatitis. I do not for a moment believe that what is presented constitutes

a "vision" of the entire beast. A study of this type calls for the greatest conservatism and caution in its interpretation. The variables, intangibles and ill definables are numerous and make it difficult for one to establish adequate yardstick controls against which to measure and compare results.

The number of children in the study is not large enough to draw more than a few simple statistical deductions based on certain suggestive differences. The nature of atopic dermatitis is such that it tends to fluctuate in intensity and to improve gradually and evenually to disappear. Excluding infantile atopic dermatitis from this study removes from consideration an age group of high incidence of appearance and disappearance of symptoms. The number of children—only two out of 20—in the control group who became symptom free may simply reflect my personal inability to manage atopic dermatitis with so-called "orthodox" treatment, and that group may therefore in itself provide an unsatisfactory control for comparison with the group in which treatment was based on coping with maternal rejection. The foregoing are a few among many critical thoughts that have arisen in an attempt to interpret the results of the investigation. Regarding this preliminary exploration of human relationships, emotional reactions and behavior patterns of the child with atopic dermatitis and his mother, impression rather than dogmatism can be the only basis for comment.

It appears that atopic dermatitis in children is in most instances associated with a child with a characteristic temperament and with a mother whose witting or, more frequently, unwitting attitude to that child is one of rejection. Further, it seems that the attitude of the mother to this sensitively made child has some etiological significance in precipitating, aggravating and perpetuating the dermatitis.

English [20] has recently reemphasized that "The need for love is one of humanity's greatest hungers, and many other emotions are dependent on it." He points out the "hunger" for love, the greater need some persons have for it than others and the anxiety, expressing itself in both psychic and somatic components, which its lack produces. Lack of love disturbs the individual's sense of well-being and thereby engenders hostility and a desire to retaliate. Goresky [21] refers to the importance of expressed, demonstrative love in the family group as an essential for the maintenance of physical and mental health among all the members.

In a review of the child-mother relationship in the 33 children with atopic dermatitis it is difficult to delineate clearly a cause-effect mechanism. Four prominent features were evident, however, and they appeared to be related sequentially as follows: An atopic child with an inordinate hunger for affection finds himself confronted with a mother who unwittingly is not satisfying this need; the child as a consequence experiences distress (anxiety) and hostility, the former exhibiting itself somatically at the characteristic skin sites as the pruritus and dermatitis of atopy and the latter expressing itself psychically as wilful, resistive behavior toward the mother.

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20. English, O. S.: Role of Emotion in Disorders of the Skin, Arch. Dermat. & Syph. **60**: 1063-1076 (Dec.) 1949.

21. Goresky, V. B.: The Quick Technique of Mental Therapy, Vancouver, B. C., Canada, Wrigley Printing Co., 1949, p. 154.

This sequence conforms to that referred to by English as occurring in situations where there is a lack of love. It is suggested that this behavior and attitude pattern experienced and established in early childhood may explain the repressed hostility to a mother or mother figure found in adults with atopic dermatitis by Walsh and Kierland.[13] It is suggested this adult reaction has as its basis maternal rejection in infancy and early childhood.

Maternal rejection has been defined variously by different authorities. In a restricted sense, and with supporting evidence, Newell [18a] defined it as "that situation where the birth of the child was unwelcome to the mother." In a broader sense, Figge [17] states that "a rejecting mother is one whose behaviour toward the child is such that she consciously or unconsciously has a desire to be free from the child and considers it a burden." In this study the rejection did not take the form of overt neglect but was, rather, an accumulative effect of a continuing irritability toward the child expressing itself as frustrating nagging and scolding, emotional explosions and "scenes," unreasonable discipline, insistence on petty regimenting detail, an attempt to overpower the child's will, a running battle each mealtime over eating habits and, above all, a striking lack of demonstrative love expressed by the enfolding arms, the loving caress and the "soft word" that "turneth away wrath" (hostility).

Mohr and co-workers [16] stated that

> common features in the family constellation of the asthmatic child have impressed us strongly. The mothers . . . [exhibit] certain characteristic traits and attitudes with remarkable uniformity. They are highly narcissistic women, ambitious for themselves and children—they present ambivalent and rejecting attitudes toward their children—the mothers consistently dominate the domestic life.

The fathers are described as being passive personalities "not actively interested in their children . . . [who] play a relatively unimportant role in the training and care." In the study now being presented, the picture of the family group could not be as sharply depicted but the general resemblance to the above description was more than coincidental.

It cannot be too strongly emphasized in this discussion that the comment on maternal rejection associated with atopic dermatitis must not in any way be interpreted as an indictment, directly or indirectly, of the rejecting mother, nor should the pointing out of the possible role of this rejection in the etiology of atopic dermatitis be construed as a criticism of the mother. Figge [17] and Newell [18b] have clearly analyzed the factors which predispose to and motivate the rejection, and this point should be underlined: Many of these factors are beyond the mother's control. Usually the mother is an unwitting and innocent victim of circumstances which place her in this rejecting role. All the foregoing material is particularly apropos in relation to the physician's manner toward the mother of the atopic child. In commenting on "the essential attributes of the physician dealing with functional dermatoses," Obermayer [22] rightly insists that "intelligent sympathy and understanding are the two prime requirements." Lamb [23] recently outlined five rules

22. Obermayer, M. E.: Functional Factors in Common Dermatoses, J. A. M. A. **122**:862-864 (July 24) 1943.

23. Lamb, J. H., in discussion on Gottesman, A. H., and Menninger, K.: The Dermatologist and the Psychiatrist, Arch. Dermat. & Syph. **59**:372 (April) 1949.

which serve as a useful guide to the dermatologist in the management of a problem in which the emotional elements are prominent:

> the dermatologist should (1) take adequate time to listen . . . (2) confine his therapy to simple and superficial methods, (3) build up the patient's self respect and self confidence, (4) relieve environmental hazards . . . and (5) point out more mature approaches to life's problems, whenever possible.

These wise words are of the utmost help in counseling the distraught mother of a nocturnally flexure-scratching child.

In bringing this comment to a close, I will make reference again to the complexity of the etiological factors in atopic dermatitis. This has been recognized by all who have become engrossed by the enigma of its pathogenesis. Brunsting,[24] in the analysis of a large group of patients, has recorded the multiplicity of these factors. The proponents of various etiological mechanisms have, in their enthusiasm, perhaps had a tendency to make claims on an uncertain factual basis. I fear that I have not escaped this pitfall entirely. The principal purpose of this paper has been to draw attention to the unusual features of the child-mother relationship in most instances of atopic dermatitis. Saxe's aforementioned poem, the theme of which has continued to permeate my thoughts throughout this study, perhaps pertinently summarizes the disputatious aspect of atopic dermatitis and its pathogenesis:

> And so these men of Indostan
> Disputed loud and long,
> Each in his own opinion
> Exceeding stiff and strong,
> Though each was partly in the right,
> And all were in the wrong!
>
> So oft in dermatologic[25] wars,
> The disputants, I ween
> Rail on in utter ignorance
> Of what each other mean
> And prate about an Elephant
> Not one of them has seen!

SUMMARY

During recent years the concept of "humanism" in medicine has become increasingly associated with the scientific viewpoint. A growing study of the tangible somatic expressions of emotional interpersonal relationships is a part of this increasing association. There has been an increasing reexamination of unexplained or partially understood dermatoses in which emotional factors have been evident. Atopic dermatitis belongs to this group of dermatoses.

The mother is the closest and most prominent personality in the environment of the infant and growing child. Maternal rejection has been shown to be a usual observation in children with clinical forms of atopy. Repressed hostility to the mother or a mother figure is present in most adults with atopic dermatitis.

In this study of a group of children with atopic dermatitis the common observation of maternal rejection was confirmed. It is suggested that this rejection by the

24. Brunsting, L. A.: Atopic Dermatitis (Disseminate Neurodermatitis) in Young Adults: Analysis of Precipitating Factors in 101 Cases and Report of 10 Cases with Associated Juvenile Cataract, Arch. Dermat. & Syph. **34**:935-937 (Dec.) 1936.

25. With apologies to the poet.

mother elicits in the child anxiety and hostility, which have two components of expression—one, the somatic component, exhibiting itself as the characteristic pruritus of atopic dermatitis, and the other, the psychic component, exhibiting itself as wilful (aggressive) behavior. A program of therapy, directed mainly toward the correction of the mother's behavior to the child, is outlined. It consists of instructing the mother concerning (*a*) the basic emotional needs of a child, (*b*) the effect on the child of these needs' not being provided and (*c*) the means of providing them.

A comparison is made between a group of children treated by indirection in this manner and a control group of children not treated thus. The results of this study suggest that the management of the maternal rejection factor in children with atopic dermatitis is an important adjuvant to existing therapeutic procedures.

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ABSTRACT OF DISCUSSION

Dr. Earl D. Osborne, Buffalo: I am going to discuss the subject of atopy in children with a great deal of fear and trembling. I feel, I can assure you, that the description of the subject as the "wondrous elephant" is very well taken. I want to emphasize what Dr. Williams makes perfectly clear in his paper, that he is covering one of the many facets of the psychogenetic approach to atopic eczema in young children and infants over 1 year of age. He does not include a discussion of infantile eczema in babies or infants under 1 year of age.

I believe that dermatologists are inclined to be realists as a group in spite of the fact that some of our distinguished members have been the leaders in the presentation of the psychogenic aspects of atopy. I think that most of us are inclined to seek for concrete causes for atopic dermatitis, such as known definite allergies of one type or another, in explaining physical effects.

It is well that we have these various facets of the psychogenic aspects presented to us from time to time. I can assure you that it gave me a great deal of stimulation along this line to read Dr. Williams' paper.

Now I'll mention some of the thoughts that have come to me after reading the paper and some things that I have done in checking up on some of my impressions: In the first place, I am sure all of us have had experiences in real life in which a psychogenic experience of one type or another has led to a miraculous cure when least expected in atopic dermatitis. I have observed three such instances, and doing so proved to me, with other observations, that, whether we like it or not, there is a definite psychogenic mechanism that affects the neurocirculatory mechanism and certainly is one of the trigger mechanisms in inducing an atopic dermatitis.

Two years ago, in considering this subject with a group of psychiatrists in my county, I took the other side and presented all the arguments against the psychogenic factors in atopy as a whole and particularly in atopic dermatitis, and when the discussion was all over the leading psychiatrist said, "I think you have all had a demonstration of a forceful, dynamic individual expressing one, two, three, four how these subjects should be handled." He added, "I think we should all realize that is the best form of psychotherapy in handling these cases."

Dermatologists are inclined to give specific directions, one, two, three, four, and that method is good treatment according to the angle of the psychiatrist. Furthermore, I am convinced that the dermatologist is the better psychiatrist in handling these cases. I think Dr. Williams emphasizes that. I have had unhappy experience in referring these patients to psychiatrists. I have yet to see an excellent result or even a good result obtained by treatment by a psychiatrist.

In thinking over some of the problems of atopic dermatitis I thought it was well from my own standpoint as well as in discussing this paper to review the normal course of atopic

dermatitis in general, and in doing so I went over 200 records of cases of atopic dermatitis, all in persons past 1 year of age. I want to point out some things that I think are typical of the group. In the first place, I am satisfied—my associates and I published this observation some years ago, and it has since been confirmed— that if patients in this age group are hospitalized in allergy-free rooms in a hospital well over 90 per cent of them will have clearing within two to four months.

Furthermore, in 11 per cent of the cases the onset is in summer; in 89 per cent the onset is in winter. In examining the patients my associates and I found that 16 per cent of the cases developed in summer, but nine of them were later proved to be due to hypersensitivity to wool. In analysis of the 100 cases it was found that 34 per cent had a history of clearing in summer, 36 per cent of improvement, decided improvement, in summer but not clearing, and 30 per cent, of the same condition in summer as in winter. That observation brings forth a significant point. I think that as dermatologists we should all dwell on the factors that cause these persons to have clearing in summer. There must be some reason that 70 per cent have clearing in summer.

I have done a great deal of thinking about this point—and testing, observation and, in the last 12 years, a great many determinations on wool content of dust. I am convinced that we still do not pay enough attention to the content of wool in house dust, in ordinary house dust on shelves and bureaus and so forth, the material that floats in the air as the principal inhalant allergy agent in these cases. Examination of samples of house dust at monthly intervals will give a great deal of information with regard to atopic dermatitis. I am unprepared to say what the percentage is, but I am certain that the wool content of house dust provides the principal explanation for much of the clearing which these patients experience in summer.

In another group of 50 patients, from 5 to 15 years of age, 26 per cent had clearing for two or three years between the ages of 1 and 5. That figure is significant. These patients are inclined to have clearing for two or three or four years and then have a recurrence later. Also, the figure for spontaneous clearance without any recurrence is somewhere between 10 and 20 per cent, and when you add that to the figure of 26 per cent for clearing from one to three years between the ages of 1 to 5, you get a figure that is dangerously close to the 45 per cent that Dr. Williams gave for clearing after treatment. In other words, a normal experience with atopic eczema must be borne in mind at all times in evaluating the success of any form of treatment.

I think as dermatologists we should all pay more attention to the psychogenic approach in atopic dermatitis. Perhaps we are so constituted that only a certain percentage of all dermatologists are properly fitted to examine into the psychogenic aspects of the problem. I am sure that psychogenic factors are among those that act as a trigger mechanism in inducing an active clinical manifestation.

DR. SAMUEL M. PECK, New York: I wish to express my admiration and thanks for this paper. I believe that the time has come when dermatologists can evaluate the success of the psychotherapeutic approach in our field, especially as it concerns the so-called all-comprising group of the eczemas.

It is my conclusion that there are few cases which can be cured by the psychosomatic approach only. Such cases are striking and include those which have given us our most conspicuous failures with the orthodox approach based on control of a mechanism of allergy. However, there are many cases in which the fundamental allergic mechanism is the initiating etiological factor, and on this background we have superimposed all those involved factors which have been discussed today. I believe that it still has to be proved that the allergic mechanism as such is either initiated or profoundly influenced by psychosomatic factors. Perhaps it is an oversimplification to state that it seems that it is the threshold of response in the allergic person which is most profoundly affected by psychosomatic influences.

DR. S. WILLIAM BECKER, Chicago: Dr. Williams is certainly to be congratulated on this excellent presentation of, as Dr. Osborne said, one of the facets of this difficult problem. I made the rounds with a prominent dermatologist in a large city hospital a few years ago, who, as he came to a child with this disorder, said, "The practice of dermatology would be a pleasure if we did not have to take care of these children."

I think that Dr. Williams' statements apply not only to atopic dermatitis but also to any of the functional diseases, whether dermatological or otherwise. Dr. Williams has chosen a severe test, because Comby and Marfand, French authors, years ago stated that the earlier in life functional diseases appear, the more difficult they are to relieve. I have been accused by the psychiatrist of generalizing too much, but it seems to me that if you take the time to sit down and talk to patients with any of the neurodermatoses you will find that all these persons are, at least, very similar. The problem goes back to the fact that two overactive, oversensitive persons marry each other. A genius in the hills of Kentucky doesn't stay there; he goes "over the hills." He goes into business or to school and becomes an attorney or a physician, and when he looks for a marital partner he doesn't go back and marry the little girl whose books he carried to school but chooses a girl of the same active type. Therefore, the children cannot help being unstable because they are chips off two oversensitive blocks.

I am rather convinced that all children of overactive parents are rejected because the mother is immature. You may have read the series of articles on divorce in the *Saturday Evening Post* not many months ago. The chief cause for divorce was given as emotional immaturity. The mother marries the wrong man, and pretty soon she has a baby. By that time she is to a certain extent disappointed in her husband, as all wives are at some time or another.

She has to have some other outlet; so here is this animated doll that she can play with and have fun with in a continuation of her childhood. She ties up emotionally with the children because, of course, the children do not talk back to her and they don't do the bad things that husbands do. But in doing so she is keeping her emotions on an immature level, and I think the point made by Dr. Williams, of the necessity for maintenance of a healthy relationship with the husband, is extremely important.

I have had hundreds of patients read the chapter on children in "The Prophet," by Kahlil Gibran, in which the author tries to give an unbiased, dispassionate attitude toward children. He says that your children are not your children. They come through you, but they do not belong to you. Also he says you should not try to inflict your old-fashioned ideas on your children but try to learn from them because they are members of the next generation and time always goes forward and never backward.

In other words, we should not take our children too seriously. I am sure Dr. Williams also has had difficulty in putting across this viewpoint. It is hard, at least in a brief period, to convince women they should change their ways. There are premarital courses given in many universities which may give us some help in this particular problem. However, these courses are not always given by men with family experiences.

It is not only the mothers; sometimes the fathers are at fault. I recently had a patient with three small children, who said, "Why, Doc, I wouldn't think of going any place without my three daughters." He said nothing about his wife. I presume he leaves her at home and goes out and has fun with his children. He thereby keeps his emotions on an immature level.

The discussions by Dr. Peck and Dr. Osborne remind us that we must realize that allergies do play a part in these difficulties. Climatic changes play a great part. I think the particular climatic changes which have been so well described by Peterson at the University of Illinois and Mills at the University of Cincinnati have much to do with the fact that the condition clears in the summer and is worse in winter. Many of these children have clearing maybe for one summer, but each year the dermatitis becomes a little severer until finally the patients have it the year around.

DR. GEORGE W. BINKLEY, Cleveland: We are indebted to Dr. Williams for accenting the maternal rejection factor in infantile atopic dermatitis. Dr. Williams' series of successes in 31 of 33 cases of atopic dermatitis demonstrates that he is adept in the psychosomatic approach.

For those of us who have little facility in office psychiatry the other therapeutic measures in the management of atopic dermatitis will remain prime. None will deny that the basic problem in atopy is the allergen contacting a sensitized individual. This reaction is productive of histamine and an atopic dermatitis. Just as the catalyst nickel accelerates the chemical reaction of cottonseed oil with hydrogen to produce crisco,® so the maternal rejection, in my opinion, is a catalyst in producing atopic dermatitis. Other catalysts of importance are cold, strong detergents, fatigue, infection and trauma, often in the form of scratching.

To combat the acceleration of the atopic reaction one can use many therapeutic agents, all of which tend to mitigate and relieve. The important agents are Dr. Williams's contribution, controlling the maternal rejection, and provision for adequate cutaneous warmth, use of sulfonated oils for cleansing, rest—that is, additional rest—use of antihistamine drugs, splinting or protection of the skin to prevent trauma and application of all the topical therapy, including the use of tars, ultraviolet irradiation and superficial roentgen irradiation.

Dr. Louis A. Brunsting, Rochester, Minn.: A child who is disfigured by atopic dermatitis is an object of concern not only to himself but to those closely associated with him, his siblings and playmates, and his psychological reactions are intensified by the cruel rebuffs that he meets with and the rivalries that are set up. Dr. Williams has brought out the factors concerned in maternal rejection, which form only one aspect of the psychiatric problem. In the tempo of modern living there is a tendency to shift away from the solid anchor of the quiet home environment and the counsel of the pastor and the old time general practitioner. We cannot expect professional educators in our schools, camps and special institutions to take the responsibility for the management of these children, which belongs in the home. As dermatologists we should be slow to yield to the temptation to explore aberrations in the field of psychiatry. We may realize that abnormalities exist, but if we venture too far beyond our province we may lift the lid of Pandora's box and cause more confusion than existed originally. The management of psychiatric problems of atopic children is best conducted in cooperation with an understanding psychiatrist.

Dr. Howard Hailey, Atlanta, Ga.: This is the finest presentation of the subject it has been my privilege to hear at any medical meeting. I wish more of us were able to present this subject in such a clearcut fashion. I want to heartily endorse Dr. Brunsting's remarks.

I should like to emphasize the necessity of care of the skin in infants with eczema. The mother is instructed to discontinue general bathing. The body folds are cleansed with warm water and castile soap sparingly. A good quality borated talc is used freely two to four times daily. Only 100 per cent cotton clothing next to the skin is allowed.

The mother and any other nurses for the baby are instructed to discontinue use of nail polish, perfume and other cosmetics while in charge of the baby. The mother, when possible, should have a daily minimum period of two hours of freedom from the baby. The father of the patient is told to keep the baby's skin protected from his woolen clothes by the use of a large cotton napkin. He also must wash his face and hands thoroughly when he comes home from work before handling the baby.

In the past I know that I have been guilty of overtreating these children. The less one treats them and the cooler one keeps them, the better they will get along and the quicker they will recover. It is a crime to subject these infants to skin tests for "allergy." These tests are of no value in the intelligent management of eczema in infants. Patch testing in adults against contact dermatitis is entirely another question.

Dr. F. J. Eichenlaub, Washington, D. C.: As I listened to this paper and the discussion I wondered whether any of us remembered the fact that infantile eczema existed before there was psychotherapy, before there was soap and before there was too much nail polish in the world.

Dr. H. E. Michelson, Minneapolis: I believe the discussion should stick strictly to the topic of the essay, and I shall therefore confine my remarks to that.

We have heard about the mother's being at fault or the father's being at fault, but, as a matter of fact, the real trouble is the eczema. A family would probably get along very nicely if the child did not have eczema, and since the eczema goes on the tensions increase and cannot be laid to any other cause than the disease itself. We all know an atopic person is atopic for life. We see many phases, and, although I have heard in this discussion the words "clear up," I have not heard the word "cure."

I think sympathy for the child is a fine thing, but sympathetic management is much more important, for these children must be raised to live in this world. They are not going to live in an isolated atmosphere manned by trained parents. It is much more important that they become self reliant persons and be able to live independent lives. If the mother makes the child dependent on her love, he is going to be in a very bad way when he does leave home.

One thing that has not been discussed here is the problem of the atopic alcoholic, which is a very great problem, as all dermatologists and psychiatrists know. As Dr. Brunsting said, we must not become amateur psychiatrists. There is a great difference between dealing with psychiatric problems and being a psychiatrist. The purely psychiatric treatment must not be confused with the so-called supportive psychic therapy that all physicians supply.

Another point that has not been mentioned is the fact that atopic eczema is a familial affair—if a mother who has had atopic eczema cannot understand the poor baby, who in the world can?

I think that all these factors mentioned are merely going around the central problem, which is eczema, and one of the great questions that dermatology has to answer today is, what is atopic eczema?

DR. DONALD H. WILLIAMS, Vancouver, B. C., Canada: I am very grateful to the discussers for the numerous points raised, which emphasize the difficulty of arriving at a common ground on the basic etiology of atopic dermatitis. The fundamental cause still remains elusive. The solution of the enigma undoubtedly will await further refinement in our biochemical and biophysical investigative technics. Until the day of complete enlightenment arrives we must continue to bring to the vast unknown of atopic dermatitis the existing little candles of our therapeutic knowledge.

DANGERS INVOLVED IN DYES, COSMETICS AND PERMANENT WAVE LOTIONS APPLIED TO HAIR AND SCALP

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WHEN ONE considers the worldwide use of cosmetics for the scalp and the relatively few harmful effects seen by dermatologists in the last few years, one appreciates the value of the regulatory measures legalized by Congress in the Federal Food, Drug and Cosmetic Act of 1938. The increase of education and regulations for operators of barber shops and beauty parlors has minimized the dangers for the patrons but has not helped the operators. In recent years in my practice I have seen many operators suffering from occupational dermatitides. These eruptions are due not to one sensitivity but to a combination of factors. The *Industrial Hygiene Newsletter* mentions that three hairdressers exposed to thioglycolic acid have been studied. Interest in this subject continues because of the case of a hairdresser with aplastic anemia, believed to be of chemical origin, which has been followed carefully for the last two years.[1]

Apparently the trend is to do away with barber shops and beauty parlors, for nowadays all their arts can be practiced at home. Hence most of the untoward reactions from scalp cosmetics result from carelessness, overuse or misuse of the product, due to failure to apply the agent according to directions.

The dangerous agents might be classed as mechanical or chemical. The use of metal clips, plastic combs and brushes tends to break the hair. Metals cause dermatitides, especially in the occipital areas. As regards the chemicals, most of the dangerous or irritating ones have been removed by the industry, but it is impossible to remove all the sensitizing substances. There will always be the hypersensitive person susceptible to a specifically active substance. When a physician who performs innumerable patch tests over the years notes their sensitizing ability, he marvels that there are not many more contact dermatitides from repeated use of cosmetics. If human beings seriously considered the possible risks in the use of cosmetics fewer would use them, but knowledge will not deter the seeker of beauty, even the female dermatologist.

These sensitizers are numerous—the essential oils in bay rum, the synthetic perfumes in brilliantine, the various oils and gum resins in hair creams and curling applications. The many scalp lotions and tonics, despite ridicule, are still popular with the male sex. They contain irritants and sensitizers, namely, pilocarpine,

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1. Thioglycolic Acid Exposures, Indust. Hyg. Newsletter **10**:6 (Feb.) 1950.

cantharides, quinine, acetic acid, camphor, capsicum, betanaphthol, resorcinol, chloral hydrate, rosemary oil, bergamot oil and numerous other essential oils and chemicals. Shampoos have a tremendous popularity and contain perfume and sulfonated mixtures which may sensitize a susceptible person. The coconut oil shampoos are perfumed with several stable synthetic and essential oils. Hair dyes and so-called rinses are the oldest but still the most dangerous hazards of the hairdresser's trade. Copper, lead, silver, pyrogallol, iron and potassium permanganate have been replaced by paraphenylenediamine and similar compounds.

The introduction of the cold permanent wave processes has created the most recent hazard. The machine type (hot) method formerly popular caused occasional electric burns due to the carelessness of the operator or a faulty machine. The machineless (cold) method can cause local skin irritation and is still under suspicion as being able to produce systemic effects due to thioglycolic acid.[1] There are many confusing and contradictory reports concerning the possibilities

TABLE 1.—*Reactions to Patch Tests with Ammonium Thioglycolate and Thioglycerol Lotions in Those Having Histories of Previous Dermatitis and Exposure to Cold Wave Solution*

Negative Reactions to All Tests	
Those having had ivy dermatitis	28
Those having had other skin disorders	11
Those having had exposure to cold wave solution	53
Reaction to Original Test Negative; to Repeat, Positive	
Those having had ivy dermatitis	17
Those having had other skin disorders	6
Those having had exposure to cold wave solution	26
Reactions to Both Original and a Repeat Test Positive	
Those having had ivy dermatitis	20
Those having had other skin disorders	4
Those having had exposure to cold wave solution	22

for injury to the hair and scalp from cold wave processes.[2] The report of the American Medical Association Committee on Cosmetics [3] states that "Thioglycerol is also an efficient agent, but because of manufacturing difficulties its use has been limited. Large volume production is now possible, and thioglycerol may assume greater commercial importance." In view of this report it seemed that comparative

2. Laug, E. P., and Draize, J. H.: Percutaneous Absorption of Ammonium Hydrogen Sulfide and Hydrogen Sulfide, J. Pharmacol. & Exper. Therap. **76**:179 (Oct.) 1942. Bunce, A. H.; Parker, F. P., and Lewis, G. T.: Accidental Death from Absorption of Heatless Permanent Wave Solution, J. A. M. A. **116**:1515 (April 5) 1941. Cotter, L. H.: Thioglycolic Acid Poisoning in Connection with the "Cold Wave" Process, J. A. M. A. **131**:592-593 (June 15) 1946. Goldman, L.; Mason, L., and McDaniel, W.: Permanent Wave Process: Clinical Report with Special Reference to the Effect of Ammonium Thioglycolate on the Skin, J. A. M. A. **137**:354-357 (May 22) 1949. Behrman, H. T.; Combes, F. C.; Weissberg, G.; Mulinos, M. G., and Hurwitz, M. M.: The Cold Permanent Hair-Waving Process: A Dermatologic and Clinical Study, J. A. M. A. **140**:1208-1209 (Aug. 13) 1949. McCord, C. P.: Toxicity of Thioglycolic Acid Used in Cold Permanent Wave Process, J. A. M. A. **131**:776 (June 29) 1946; The Physiologic Properties of Thioglycolic Acid, Indust. Med. **15**:669-676 (Dec.) 1946. Howell, J. B.: Contact Dermatitis from Cold Permanent Waving, Arch. Dermat. & Syph. **49**:432 (June) 1944.

3. Lehman, A. J.: Health Aspects of Common Chemicals Used in Hair-Waving Preparations, J. A. M. A. **121**:842-845 (Nov. 19) 1949.

results of patch tests with thioglycerol and ammonium thioglycolate lotions might be interesting. To avoid entering the controversy I will merely cite the results of these patch tests.[4]

Patch tests were done on 223 subjects to observe the irritating and sensitizing action of these chemicals. With the exception of one male, the subjects were women ranging from 18 to 34 years of age. All were healthy persons with normal skin. History of allergic tendencies or skin disturbance was taken before the tests were made. Sixty-five of the group gave a history of previous dermatitis due to plants, whereas 21 had had some other type of cutaneous disturbance. It was found that 101 had had previous exposure to cold wave processes.

TABLE 2.—*Procedure Used in Patch Testing with Ammonium Thioglycolate and Thioglycerol*

Subjects
No.—223 (1 male)
Age—18 to 34 years
History of Dermatitis
Ivy—59
Other—21
Composition of Ammonium Thioglycolate Lotion
0.55 N; pH 9.3 with excess ammonia
Composition of Thioglycerol Lotion
0.55 N; pH 9.3 with acetic acid and ammonia
Application of Patches
Site—Inner aspect of upper arm
Original—1 test with thioglycerol and ammonium thioglycolate to each arm
Repeat—2 tests with thioglycerol and ammonium thioglycolate to each arm

TABLE 3.—*Original Test Reaction in 223 Subjects* *

No. of reactions to thioglycerol	20
1 temporary immediate followed by delayed	
No. of reactions to ammonium thioglycolate	24
No. of reactions to both substances	8

* Two subjects refused further tests because of severe reactions.

PROCEDURE OF TESTING

Elastopatches and kleenex® pads were used to apply the solutions. With a 1 ml. graduated pipet 0.1 ml. of the test solution was placed on each pad. The ammonium thioglycolate solution was approximately 0.55 N, buffered to a pH of 9.3 with excess ammonia. Other ingredients were merely emulsifying materials. The thioglycerol lotion was 0.55 N, buffered to a pH of 9.3 with acetic acid and ammonia. With the exceptions noted the thioglycerol lotion was the same as the ammonium thioglycolate lotion.

On the first application one patch was applied to the inner surface of the right upper arm and the other to a similar site on the other arm. The patches were removed at the end of 48 hours, at which time and at approximately every 48 hours thereafter the reactions were read. Two weeks after the first application the patches were reapplied to the same areas. An additional patch was applied to each arm, testing the other lotion. For example, if on the first application the thioglycerol lotion was applied to the right arm, it would be applied to the same arm on the second application, and adjacent to it, the ammonium thioglycolate lotion. This procedure was employed so that any change in the irritating effect from one time to another might be noted.

4. Dr. Paul J. Catinella assisted in the performance of the tests.

RESULTS

In the original test there were 20 reactions to the thioglycerol lotion. One immediate reaction subsided and was followed by a delayed reaction. There were 24 reactions to the ammonium thioglycolate lotion. Eight subjects reacted to both substances. Two refused to submit to further tests because of the severe reaction.

Retests were done on 213 subjects and resulted in 76 reactions to the thioglycerol lotion. These included 36 immediate, 7 immediate followed by delayed and 33 delayed reactions. There were 26 reactions to the ammonium thioglycolate, 25 being immediate and 1 immediate followed by a delayed reaction. Sixteen subjects retested reacted to both lotions. The so-called delayed reactions occurred six to nine days after the patches were applied. They developed rapidly and consisted in solid, round, raised and extremely itchy lesions measuring about twice

TABLE 4.—*Repeat Test Reactions in 213 Subjects* *

No. of reactions to thioglycerol	76
36 immediate	
7 immediate followed by delayed	
33 delayed	
No. of reactions to ammonium thioglycolate	26
25 immediate	
1 immediate followed by delayed	
No. of reactions to both substances	16

* Delayed reactions appeared six to nine days after tests and were solid, round, raised, flat and very itchy areas twice the size of the test area. One patient again tested to thioglycerol showed a severe vesicular, exudative reaction.

the size of the patch applied. One of the subjects who acquired such a reaction to thioglycerol submitted to retesting with this substance and showed a severe vesicular and exudative reaction.

It is apparent that both of these solutions have an irritating plus a sensitizing action. The thioglycerol lotion, however, is a far more potent sensitizer than the ammonium thioglycolate lotion. In general, the reactions to the former were severer, more prolonged and more constant than those with the ammonium thioglycolate.

CONCLUSIONS

Patch tests with thioglycerol and ammonium thioglycolate lotions were done on 223 subjects to observe the irritating and sensitizing action of these chemicals. The reactions to the thioglycerol lotion were severer, more prolonged and more constant than those to the ammonium thioglycolate lotion.

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PECULIAR NAIL ANOMALIES

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THE NAILS afford an apparently easy field for investigation. Much might be revealed by their anomalous manifestations, especially in regard to internal disorders. Unfortunately, the influences behind their deviations from the normal still remain obscure.

Normal or abnormal shapes of the nail originate from the matrix and persist while the nail is attached to its bed or when it becomes a piece of inert horny structure, solidly or loosely attached, like a hair to the scalp.

NAIL EN RAQUETTE

One of the most peculiar among the unusual nails is the one accompanying the short and wide thumb (*le pouce en raquette* of du Bois).

"Blakiston's New Gould Medical Dictionary,"[1] describes the anomaly of nail en raquette as follows:

> A dystrophy of the nail in which the nail, usually that of the thumb, appears wider than normal, its transverse curvature diminished so that the nail seems flat. The effect is that of a miniature tennis racket.

Great dermatosyphilologists of the past believed that a perfect human specimen could not have congenital syphilis. Any deviation from the normal was put immediately into the lap of Dame Vérole. The racket thumb was included. In 1926 du Bois [2] suggested it as a minor sign of congenital syphilis, and his illustrations repeat the same suggestion in 1948 in Deseaux's [3] textbook on common dermatoses.

The thumb and/or the nail en raquette are not mentioned in the available textbooks of dermatology and syphilology either as an anomaly or in relation to syphilis, except by Deseaux.[3] Pardo-Castello [4] mentions it in his book, without comment. It is not mentioned in papers or textbooks on orthopedic surgery or bone pathology.

Read at the Seventieth Annual Meeting of the American Dermatological Association, Inc., Jasper National Park, Alta., Canada, June 19, 1950.

1. Jones, H. W.; Hoerr, N. L., and Osol, A.: Blakiston's New Gould Medical Dictionary, ed. 1, Philadelphia and Toronto, The Blakiston Company, 1949.
2. du Bois, C.: Quelques dystrophies localisées de l'hérédo-syphilis, Ann. de dermat. et syph. **7**:415 (July) 1926.
3. Deseaux, A.: Traitement des dermatoses communes: diagnostic d'après les lésions, schémas pathogéniques, topographie, Paris, Masson & Cie, 1948.
4. Pardo-Castello, V.: Diseases of the Nails, ed. 2, Springfield, Ill., Charles C Thomas, Publisher, 1941.

The literature on this anomaly seems very meager. The condition is briefly discussed by Pinetti [5] with other syphilitic dystrophies, but no opinion is expressed as to its significance. It is mentioned with other heredosyphilitic dystrophies by Mestchersky,[6] professor of dermatosyphilology in Moscow. He says, "It must be extremely rare as in all my practice I have not come across a single case."

A French comment on the subject is expressed by Simon [7] in these terms: "Poetic exaggerations began with his [Fournier's] son Edmond and his dental stigmas of congenital syphilis. Everybody wanted to have his stigmas. I will name only the funniest (*les plus curieux*): myopia, beetling eyebrows, the racket thumb, short little fingers, sternal malformations."

Périn,[8] although in disagreement with Simon [7] with regard to the benignity of syphilis, is in accord in regard to the value of the above-mentioned stigmas.

The racket thumb is not mentioned even by Milian [9] with his score of positive nail signs of occult congenital syphilis, viz., the transverse grooves particularly limited to the thumbs (*sillon transversaux; raies transversales*), the pin-pointed erosions, the lilac arch, leukonychia, black pigmentations, friability and sideration (arrest of growth of the nails). An example of congenital syphilitic nails, according to Milian,[9] would be seen in figure *7 c*.

Brachymegalodactylism (wide big fingerism) was studied from the heredity standpoint by Drinkwater,[10] Breitenbecher [11] and Hefner.[12] Breitenbecher [11] studied disproportionally short thumbs for 10 years and published reports of cases of this occurrence in five generations. Hefner [12] also reported repetition of the anomaly in five generations, appearing in half the offspring, irrespective of sex, when one parent was affected. His observation confirms the previous conclusion of Breitenbecher [11] that the trait is a pure Mendelian dominant.

Heller [13] mentions macrodactyly (big fingers) and gives a drawing of a large distal phalanx of a thumb in an idiot 8 year old girl. Other paragraph headings are microdactyly (small fingers), brachydactyly (wide fingers) and adactyly (absence of fingers), all these conditions evidently considered anomalies of known significance. An illustration of a double nail (fig. 33, p. 82 [13]) distinctly resembles a racket

5. Pinetti, P.: Contributo alla conoscenza delle distrofie localizzate degli eredoluetici: distrofie e malformazioni digitali, Gior. ital. di dermat. e sif. **75**:1755 (Oct.) 1934.

6. Mestchersky, G.: Some New Stigmata of Hereditary Syphilis, Urol. & Cutan. Rev. **34**:27 (Jan.) 1930.

7. Simon, C.: Regards sur le domaine et le pronostic de la syphilis, Bull. Soc. franç. dermat. et syph. **55**:140 (March-April) 1948.

8. Périn, L.: La syphilis est-elle une maladie bénigne? Ann. de dermat. et syph. **9**:369 (July-Aug.) 1949.

9. Milian, G.: La syphilis occulte, ed. 2, Paris, J. B. Baillière et fils, 1946.

10. Drinkwater, H.: An Account of a Brachydactylous Family, Liverpool Med.-Chir. J. **28**:408, 1908.

11. Breitenbecher, J. K.: Hereditary Shortness of Thumbs, J. Hered. **14**:15 (April) 1923. Gates, R. R.: Human Genetics, New York, Macmillan, 1948, vol. 1, p. 405.

12. Hefner, R. A.: Inherited Abnormalities of the Fingers: II. Short Thumbs (Brachymegalodactylism), J. Hered. **15**:433 (Oct.) 1924.

13. Heller, J.: Die Krankheiten der Nägel, in Jadassohn, J.: Handbuch der Haut- und Geschlechtskrankheiten, Berlin, Springer-Verlag, 1927, vol. 13, part 2.

thumb. Heller calls thickening of the distal phalanx acropachy. In the chapter on acromegaly he exhibits a large outline of a racket thumb and nail considered as an acromegalic manifestation.

The racket thumb nail (figs. 1 and 2) may be bilateral or unilateral. When unilateral it may be seen on the right or on the left. It may or may not appear in other members of the patient's family. It is a conspicuous anomaly, so conspicuous that young girls hide the thumbs in shame.

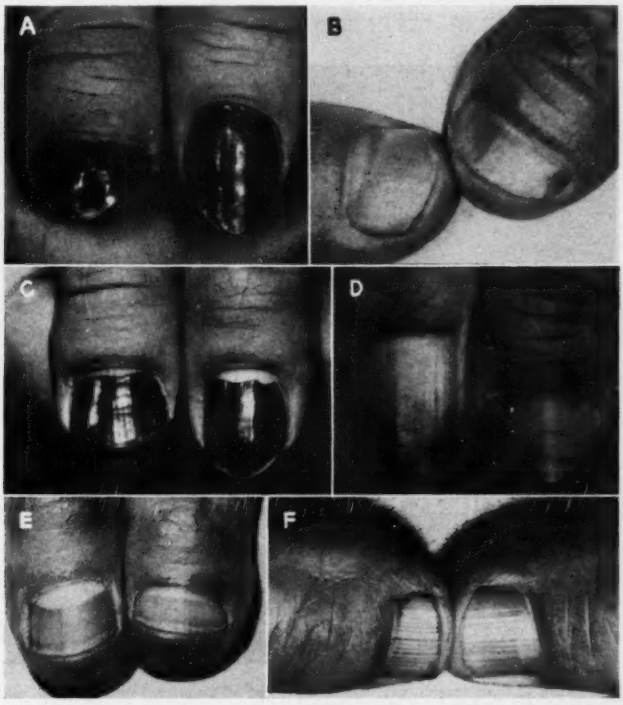

Fig. 1.—Unilateral racket thumb in young women. Notice longitudinal and transverse furrows, to account for which no past pathological factors could be found.

The anomaly was investigated in a group of 63 cases. All subjects were seeking advice for various dermatological disorders, with the exception of one female patient with congenital syphilis, or were friends or relatives accompanying a patient. Among 18 males and 45 females, both thumbs were involved in 28 and only one thumb in 34.

In nine males and in 14 females the left thumb was involved solely. In two males and nine females the right thumb only was involved.

In 31 cases data were obtained regarding family incidence of the anomaly. In the others there was no familial occurrence or it was unknown.

A paternal grandmother was affected in one case; a paternal grandfather in one case, both parents in two cases, the father in five cases, the mother in six cases, a sister in six cases, three sisters in one case, a brother in one case, two brothers in two cases, female children in two cases and a paternal cousin in two cases.

In one case the sister had the anomaly on the opposite thumb. In one case the father, a brother and a sister were affected. In one case a brother and a niece were affected. In none of the cases was the anomaly found in the patient's grandchildren.

In four cases trauma was given as the believed causative factor (sucking, biting, crushing, jamming, etc., in infancy).

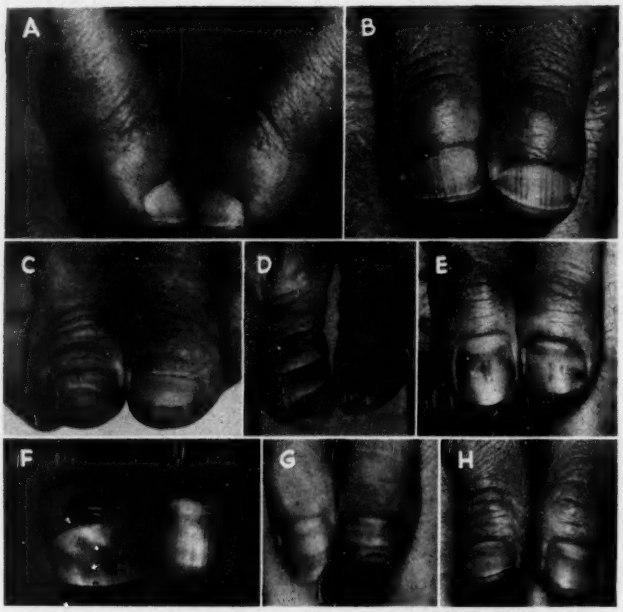

Fig. 2.—Short and wide thumbs and nails. *E*, *F* and *G*, unilateral racket thumb and psoriasis. *H*, unilateral racket thumb in a woman with congenital syphilis, the only case in a series of 63 which corresponded to Du Bois's qualifications.

In two cases there was psoriasis of the opposite thumb. In five cases there was psoriasis or severe seborrheic eczema elsewhere.

With the exception of the above-mentioned person with congenital syphilis, no patient had a positive or doubtful blood reaction for syphilis or a family history suggesting congenital syphilis.

The anomaly does not suggest any relation to any internal or external pathological condition. Its predominance in the female is remarkable. It is uncommon but not rare.

Because of the high percentage of incidence in various members of the patient's family it is reasonable to call this, like other nail anomalies discussed in this study, a hereditary phenomenon.

I have never seen short and wide big toes or toe nails. I have a male patient with a short and wide little finger nail and a supernumerary nail sprouting from the center of the finger and a woman with bilateral moderately short and wide middle finger nails, like her father's. Micronychia of all finger nails is not rare.

Two cases presented a medicolegal-industrial aspect. In one, in a young woman who had been an artificial flower maker for years, there was simulated a painful occupational unilateral racket thumb, the patient claiming the shortness of the thumb

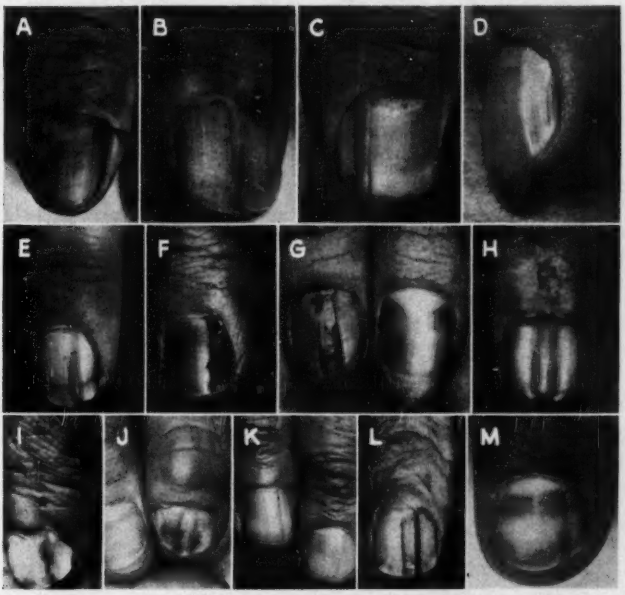

Fig. 3.—Longitudinal grooves (dystrophia mediana canaliformis Heller). In each case there was a more or less definite history of trauma, except in the condition shown in *D* and in *G*.

was due to the rolling of artificial flower stems between thumb and index finger for years. She couldn't explain why the index finger remained normal.

A man working in a file factory, where finger tips and finger nails are worn to the bleeding point, also tried to blame his work for his unilateral racket thumb. One polisher claimed the anomaly was due to pressure against the polishing wheel but did not ask for compensation.

LONGITUDINAL SINGLE NAIL GROOVE

Longitudinal single nail groove (dystrophia mediana canaliformis Heller) is a peculiar anomaly characterized by a deep single groove longitudinally located, not always on the middle line, as the "mediana" would indicate (fig. 3). In four of my

cases the groove was distinctly lateral (dystrophia lateralis canaliformis or dystrophia unguium laterosulcata).

Robinson and Weidman [14] report a good example of this anomaly with no evidence of trauma and with pathological study. They cite five cases from the literature. One is described by Pardo-Castello,[15] who cites another from the literature. Another case is reported by Kallós,[16] of a linear elevation or ridge, rather than a canal. Anderson [17] reports an instance, apparently never described before,

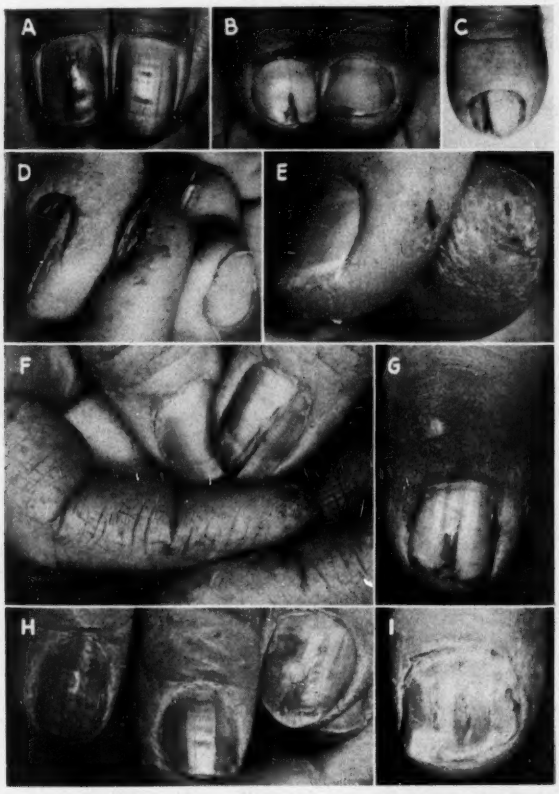

Fig. 4.—Fissures of nails and finger tips are put together to show their analogy and similar obscure mechanism of formation. *H* and *I* show psoriatic deformities resembling dystrophia canaliformis.

14. Robinson, M. M., and Weidman, F. D.: Dystrophia Unguium Mediana Canaliformis, Arch. Dermat. & Syph. **57**:328 (March) 1948.

15. Cited by Robinson and Weidman.[14]

16. Kallós, P.: Dystrophia Unguium Mediana Canaliformis (Heller), Dermatologica **96**:432 1948.

17. Anderson, C. R.: Longitudinal Grooving of the Nails Caused by Synovial Lesions, Arch. Dermat. & Syph. **55**:828 (June) 1947.

of a longitudinal groove due to the presence of a supraungual synovial lesion in the region of the nail root.

In my group of 14 cases (fig. 3), six were of definitely traumatic origin, and in three the patient had a vague recollection of injury in the remote past. In five cases the patients emphatically denied any injury. The fact that a history of injury was indefinite does not exclude its possibility as a primary factor in this nail anomaly.

This anomaly may be considered an accentuated form of the common longitudinal furrow which may appear as a groove (canaliculus, sulcus), as a ridge (ruga, corrugation) or as a fissure (slit).

Oliver and Bluefarb [18] described a case, most likely of this anomaly, under the title of nevus striatus symmetricus unguis.

Figure 3 *K* shows a case of this type, trauma having produced a median longitudinal groove and unilateral brachymicrodactyly.

Longitudinal fissuring (dystrophia longitudinalis fissuriformis) most likely is to be considered as belonging to the same group, as is also the case of Fowle and Wiggall.[19]

Dystrophia unguium mediosulcata is the name given to three illustrations in "Corpus Iconum Morborum Cutaneorum."[20] Two of them have the nevoid appearance of the cases of Oliver and Bluefarb [18] and of two of mine. They can be considered analogous to the isolated, nontraumatic fissures of the finger tips in nonlaboring persons (fig. 4), which are obscure manifestations of a local skin defect.

Montant and Eggermann [21] reported a similar and peculiar congenital longitudinal thumb nail anomaly, present in 10 members of a family of 20 and repeating itself in four generations. Half of the left thumb nail, the ulnar side, was missing. The other half was normal. The rest of the nails were normal. The radiuses and patellas were abnormal.

Transverse ridges or depressions (excluding the acute or subacute shedding in onychomadesis and the onychomycoses) never go so far as to produce a fissure comparable to the longitudinal ones (fig. 4).

However, dystrophia lamellosa unguium,[20] or onychoschizia lamellina,[4] or separation of the free edge in thin layers (fragilitas unguium, onychorrhexis), analogous to the broomlike splitting of the free end of the fragile hair (fragilitas crinium, trichorrhexis), an incapacitating disorder also congenital and of obscure origin, may be considered a form of transverse fissuring in depth.

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18. Oliver, E. A., and Bluefarb, S. M.: Nevus Striatus Symmetricus Unguis: Report of a Case with Involvement of Thumbs and Little Fingers, Arch. Dermat. & Syph. **49**:190 (March) 1944.

19. Fowle, L. P., and Wiggall, R. H.: Dystrophia Unguium Canaliformis: Report of a Case, Arch. Dermat. & Syph. **50**:267 (Oct.) 1944.

20. Corpus Iconum Morborum Cutaneorum, in Transactions of the Ninth International Congress of Dermatology, Budapest, 1935, Leipzig, Johann Ambrosius Barth, 1938, vol. 5, p. 820.

21. Montant, R., and Eggermann, A.: Syndrome héréditaire caractérisé par une hypoplasie des rotules, une malformation des radius et une hémi-atrophie de l'ongle du pouce, Presse méd. **45**:770 (May 22) 1937.

Fig. 5.—Longitudinal ridging (*A*) in a case of Addison's disease and (*B* and *C*) as seen in practically everyone from middle age on. *D*, ridging in a young man, almost in the pattern of a canaliformis. *E*, the common ridging plus psoriatic detachment.

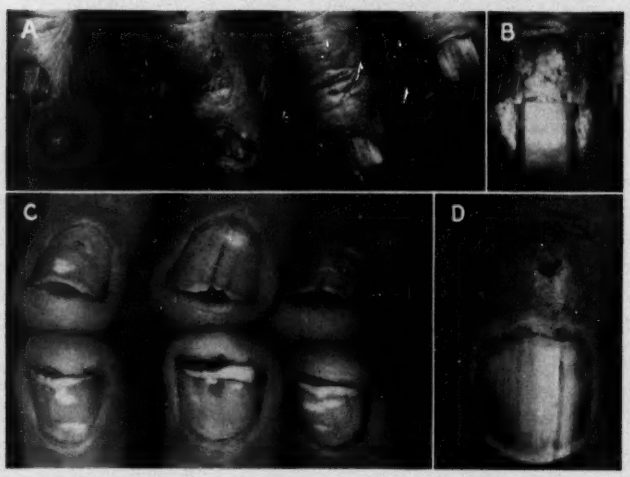

Fig. 6.—The longitudinal striations of roentgen sequelae (*A*), of Darier's disease (*C*), and with subungual hemorrhages in early Raynaud's disease (*D*). Peculiar longitudinal deformity associated with periungual warts of long standing is shown in *B*.

LONGITUDINAL FURROWS

Longitudinal furrows are usually represented by slightly raised continuous or interrupted straight, parallel, longitudinal lines (fig. 5). They are probably a manifestation of senility, very common after middle age.

Kaufman [22] studied a group of 500 men and women between the ages of 18 and 35 and found 42 (8.4 per cent) with recognizable longitudinal striations on the finger nails and 38 (7.6 per cent) with striations of the toe nails. He studied the condition histologically and found the ridges to correspond to projections of the nail bed. He came to the conclusion that the condition is common and of no significance.

Only occasionally have I seen longitudinal striations in the young, such as the case of short and wide thumb nails pictured in figure 1, in a 20 year old girl. I have seen these striations also in children, but quite rarely.

While dryness may be a cause of longitudinal ridging in roentgen radiation sequelae (fig. 6), it can hardly explain the same phenomenon in Darier's disease (fig. 6*C*) in a 14 year old girl.

The above-mentioned examples of longitudinal ridging can correctly be called onychorrhexis. This designation cannot be given to strong and healthy nails which show only longitudinal ridges, as in the group studied by Kaufman.[22]

TRANSVERSE FURROWS

Transverse furrows (Beau's lines) (fig. 7) are also common nail anomalies and are the source of much speculation in regard to their significance as a possible symptom of an internal disorder.

They have been studied histologically by Alkiewicz.[23]

White,[24] in reporting a study of 485 cases of nail disease before the American Dermatological Association 48 years ago, said, "the commonest of the constant deformities are transverse depressions, vertical ridges . . . the more unusual changes are the transverse ridges, vertical depressions."

There is no doubt that something acted on the matrix to produce the deformity. However, what this something is remains a mystery. A large number of diseases are supposed to cause the condition, which fact minimizes the value of the deformity as a retrospective sign of this or that particular disease.

When one thinks of the case mentioned by Shoemaker [25] of an overnight loss of all hair and all nails because of a violent thunderstorm, he is reminded that one has to consider the number of infinitesimal psychological stimuli during a lifetime which may account for any bodily deviation from the usual, such an anomaly possibly being later reproduced in subsequent generations.

Practically all statements in regard to diagnostic value are based on reports of single cases. As far as I know no large scale study of the anomaly has been done like that, for instance, by Kaufman,[22] on 500 cases of longitudinal furrows.

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22. Kaufman, W. H.: Onychorrhexis in Normal Individuals, Urol. & Cutan. Rev. **45**:200 (March) 1941.

23. Alkiewicz, J.: Recherches histologiques sur les sillons transversaux des ongles (Beau), Ann. dermat. et syph. **6**:36 (Jan.) 1935.

24. White, C. J.: The Clinical Study of 485 Cases of Nail Disease, Boston M. & S. J. **147**:537 (Nov. 13) 1902.

25. Shoemaker, J. V.: Diseases of the Nails, J. Cutan. & Genito-Urin. Dis. **8**:334 (Sept.); 388 (Oct.); 419 (Nov.); 476 (Dec.) 1890.

No generalization can be drawn from isolated instances. Pardo-Castello [4] cites Sabouraud as considering leukonychia an early sign of tuberculosis. This observation remains in the books as a historical datum, but transverse furrows are said to signify more. They are said to indicate retrospectively the date of a heart attack or of the delivery of a baby and to indicate cardiac infarction, intermittent claudication and trichinosis,[26] their doing so, however, being completely unknown to the cardiologist, the internist, the gynecologist and their textbooks.

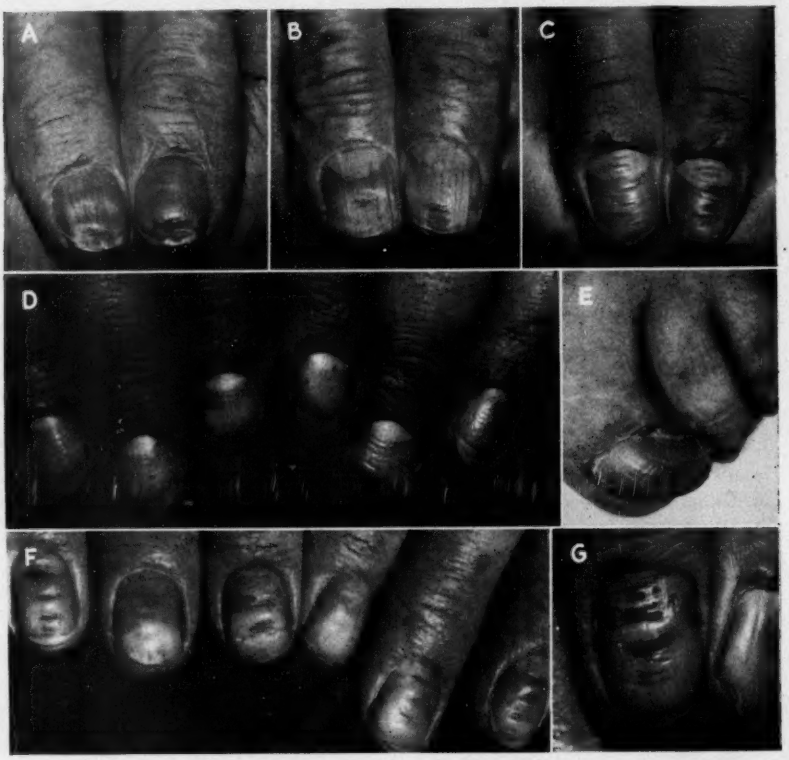

Fig. 7.—Transverse and longitudinal ridging of various shapes and appearance. The condition pictured in *B* is observed in an elderly dentist, and he gives as its cause frequent manicuring. That seen in *C* is in a healthy 17 year old girl, who thinks the Beau's lines may be due to manicuring and picking. They would fit in with the description of syphilitic thumb nails (thumb only) of Milian.[9] *F* and *G*, *depressions transversales en fossé de Simon* (Benon [26c]), for which no reason could be found, external or internal.

26. (*a*) Wiener, K.: Skin Manifestations of Internal Disorders (Dermadromes), St. Louis, C. V. Mosby Company, 1947. (*b*) Behrman, H. T.: Dermatologic Clues to Internal Disease, New York, Grune & Stratton, Inc., 1947. (*c*) Benon, R.: Le sillon unguéal transversal de Joseph Beau dans les psychonévropathies, Bull. méd. **61**:93 (March) 1947.

What are known, however, and accepted as a valuable sign are the subungual hemorrhages in subacute bacterial endocarditis.[27]

Perhaps I am prejudiced against the significance of longitudinal and transverse striations because I myself have longitudinal striae on my finger nails and Beau's waves on my toe nails and I do not consider them a significant defect. For the longitudinal ones, age may be the causative factor; I am unable to remember the date of their appearance. For the transverse lines on my toe nails I am unable to find a causative factor in my past history.

I have no figures to offer, but I can say that for many years I took special care in asking reliable, intelligent patients by the hundreds (excluding, of course, those with shedding of the nails from acute or chronic dermatitis, psoriasis, onychomadesis and the onychomycoses) how to account for the clean, smooth, normally colored transverse waves on their nails and was deeply disappointed by the inconclusive or negative answers I was able to obtain.

Figure 7 shows conspicuous transverse ridges and depressions, some in middle-aged persons and some in adolescents. They certainly have a cause, such as trauma at work or trauma from manicuring or picking and biting. Why, among the hundreds or thousands who manicure daily or bite their nails furiously, violently traumatizing the nail matrix, do only a comparative few show disfiguring transverse ridges and depressions? In some persons there may be a hereditary predisposition of the nail matrix to react to stimuli with formation of waves or canals or ridges, while the same stimuli in nonpredisposed persons may leave the matrix unaffected.

I have a patient showing deeply depressed scars, exactly in the region of the matrix, from severe chromium burns suffered in a tannery 45 years previously, and in spite of that observation the nails are perfectly smooth and apparently normal.

Apparently perfectly normal nails can be seen in cases of generalized lichen planus, psoriasis, acrosclerosis and the worst crippling manifestations of arthritis.

TRANSVERSE WHITE BANDS

Transverse white bands were described by Mees [28] in 1919 as occurring in three patients surviving acute arsenic poisoning and were promptly called Mees's lines. Mees believed they were due to actual deposition of arsenic in the nails.

Althausen and Gunther [29] in 1929 reported one case showing this condition among seven of arsenical poisoning from rat poison. The illustration is poor but the description good:

> all fingers and toenails (the latter to a lesser degree) were crossed by a white band about 3 mm. in width. The characteristic feature of arsenical poisoning, if present, is a white transverse band.

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27. Libman, E., and Friedberg, C. K.: Subacute Bacterial Endocarditis, New York, Oxford University Press, 1941.

28. Mees, R. A.: Een verschijnsel bij polyneuritis arsenicosa, Nederlandsch. tijdschr. geneesk. **1**:391 (Feb. 1) 1919, abstracted, J. A. M. A. **72**:1337 (May 3) 1919.

29. Althausen, T. L., and Gunther, L.: Acute Arsenic Poisoning: A Report of 7 Cases and a Study of Arsenic Excretion with Especial Reference to the Hair, J. A. M. A. **92**:2002 (June 15) 1929.

Simons,[30] in 1937, after reviewing the literature on leukonychia striata transversa arsenicalis, reported two cases, one in a patient with psoriasis and one in a taxidermist who ingested a great deal of arsenic while stuffing a wolf.

Four other cases of white bands in arsenical poisoning are cited by Heller.[13]

Brownson [31] in 1915 found white bands in one case of malaria. A picture from his case is reproduced by Sutton and Sutton.[32]

A case of leukonychia striata transversalis in malaria is cited by Heller.[13]

Urbach [33] describes a white band occurring after cardiac infarction in a physician.

Nekam's legends for three illustrations in "Corpus Iconum Morborum Cutaneorum [34]" read in one case "Psoriasis et leukonychia striata" and in the other two "no associated disease."

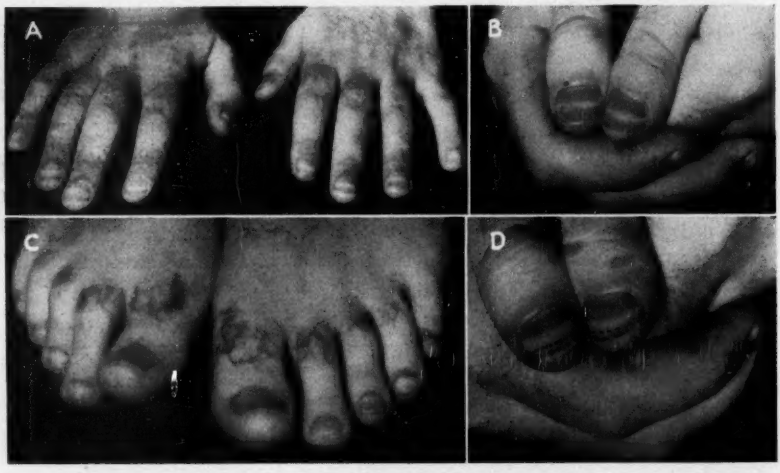


Fig. 8.—Transverse white bands in a case of Hodgkin's disease; photograph taken under difficulties at the bedside of a very sick patient. Contrast is minimal because of the extreme paleness of the patient. The bands were about two months old. The dotted lines in *D* show the place of the bands 27 days after the first photograph was taken, at the time of the patient's death.

Through the courtesy of Dr. Irving A. Beck, I recently saw a 25 year old man with Hodgkin's disease who showed 3 mm. wide perfectly straight transverse white bands in the middle of all his finger and thumb nails (fig. 8) and to a lesser degree

30. Simons, R. D. G. P.: Aanvang, duur en beloop der arseenwerking op de nagles, Nederlandsch. tijdschr. geneesk. **81**:1913 (May 1) 1937, abstracted, J. A. M. A. **109**:94 (July 3) 1937.

31. Brownson, W. C.: An Unusual Condition of the Nails in Pellagra, South. M. J. **8**:672 (Aug.) 1915.

32. Sutton, R. L., and Sutton, R. L., Jr.: Handbook of Diseases of the Skin, St. Louis, C. V. Mosby Company, 1949.

33. Urbach, E.: White Cross Striae of the Fingernails Following Cardiac Infarction, Arch. Dermat. & Syph. **52**:106 (Aug.) 1945.

34. Corpus Iconum Morborum Cutaneorum,[20] pp. 465 and 816.

in his toe nails, exactly as described by Althausen and Gunther.[29] At first it was thought the lunulae were becoming enlarged. The nail surface was perfectly smooth, free from the slightest trace of ridging or depressions either transversely or longitudinally. The white bands appeared about two months previous to the time of my observation, while the patient was having a temperature from 105 to 106 F. for two weeks and his white blood cell count was from 300 to 700. The high temperature persisted over two months.

Search for arsenic in the urine revealed none. Two weeks later the bands had moved toward the free end of the nail, and, when the patient died, 27 days after the first photograph was taken, the white bands were close to the free end, as outlined in figure 8. No new ones had appeared. The condition, or conditions, eventually provoking the white bands were still present (high fever, low white blood cell count, Hodgkin's disease). Why did no successive bands appear? In no case among those previously mentioned were successive bands described.

Pardo-Castello [4] remarks that in the many cases of arsphenamine dermatitis that he saw no one showed white bands on the nails. I do not remember seeing any in practice or mentioned in the literature as resulting from the use of neoarsphenamine or potassium arsenite (Fowler's) solution or in a medicolegal case.[35]

From these sporadic reports can one say that the transverse bands are a valuable diagnostic aid in arsenical poisoning, malaria, cardiac infarction, psoriasis and Hodgkin's disease?

CLUBBING OF THE FINGERS

Clubbing of the fingers is mentioned here only incidentally. It is the most investigated nail and finger tip anomaly. One paper alone cites 337 references [36] on the subject.

It is described as a sign of a large group of diseases and is undoubtedly of some value as an indication in disorders of the respiratory and cardiac apparatus. However, it is also described as a hereditary phenomenon in apparently normal persons, and in some cases as being unilateral.

One may assume that the ancestors of a healthy person with clubbed fingers had tuberculosis, emphysema or cardiac disease.

An interesting paper appeared recently discussing the problem of the diagnosis of an internal disorder from the clubbing of the fingers. The paper takes up an angle of the problem which, to my knowledge, has never been approached before.

Wurl [37] reports the case of a Negro who was rejected from lucrative employment three times because of his (inherited) clubbed fingers. He was told he had an "organic heart disease," that his clubbed fingers "probably meant pulmonary tuberculosis" and that he was rejected because of "heart trouble." A severe inca-

35. In a recent paper (Bureau, Y.; Rinckenbach, and Barrière, H.: Les accidents cutanés de l'arsenicisme alimentaire accidentel [ingestion de vin arsénié], Ann. de dermat. et syph. **10**:385 [July-Aug.] 1950) epidemics of arsenical intoxications from food reported in the literature are mentioned and cases are reported of 80 people with severe cutaneous and systemic manifestations from drinking arsenious wine. No mention is made of white transverse bands on the nails.

36. Mendlowitz, M.: Clubbing and Hypertrophic Osteoarthropathy, Medicine **21**:269 (Sept.) 1942.

37. Wurl, O. A.: Hereditary Clubbing of the Fingers and Toes, Mil. Surgeon **105**:217 (Sept.) 1949.

pacitating psychogenic reaction, the result of the numerous physical examinations, followed. In the hospital, while the patient was asleep or not under direct observation his respiration was normal and quiet. He became dyspneic as soon as he was approached and examined.

Assured that his respiratory and cardiac apparatus were perfectly normal, he left the hospital, cured.

This case corroborates my contention that nail anomalies are of little help as diagnostic signs and that to attempt to diagnose an internal disorder on the basis of changes in the nails may result even in disaster such as that described.

CONCLUSIONS

Nail anomalies are an interesting subject of study and speculation as to the causes behind them.

Short and wide thumb nails, longitudinal single groove (dystrophia mediana canaliformis) (Heller), longitudinal ridges, transverse ridges and depressions (Beau's lines), transverse white bands (Mee's lines) and, incidentally, clubbed fingers have been the object of this survey.

The mechanism of their formation remains obscure.

Most likely they are hereditary phenomena, like common baldness and some other conspicuous hair or teeth disorders, and may belong to the wide group of ectodermal defects.

The significance of nail anomalies as symptoms useful in the diagnosis of any particular disorder is uncertain or negative.

170 Waterman Street (6).

ABSTRACT OF DISCUSSION

Dr. F. J. Eichenlaub, Washington, D. C.: Dr. Ronchese discusses five nail dystrophies—first, the short wide thumb nail, associated with a short and thickened thumb, or racket thumb. If I have ever seen this condition, I have not noted it particularly. I can make only the negative observation that it has not been present in any case of congenital syphilis that has come to my notice.

The longitudinal nail groove has been a not too uncommon condition. Most of the cases I have seen were caused by warts or synovial cysts involving the root of the nail or presented a history of trauma. Third, the longitudinal furrows—this condition is extremely common. It may be an evidence of senility, though I personally have had the condition as long as I can remember. I have felt the condition in my case followed a severe attack of scarlet fever when I was 4 years old. While I have observed this condition frequently, I have never attached much importance to it. I do not believe it can be attributed to any one constitutional disease.

Fourth, transverse furrows—this condition also seems to occur with fair frequency. These furrows are certainly seen complicating chronic eczema of the fingers, paronychia and other diseases affecting the nail root. When they have not been associated with local disease I have been unable to correlate them with any constitutional disease. To my mind they have no diagnostic significance in relation to any constitutional disease. Fifth, transverse white bands—these too are observed not uncommonly. As far as I have observed, they are without either local or constitutional significance.

Dr. Ronchese's thesis is that the nail conditions he has presented in this paper have no significant relation to constitutional disease. I agree with this conclusion.

Dr. Frank C. Combes, New York: I was fortunate in having the opportunity to read over Dr. Ronchese's paper before his presentation. A study of diseases of the nails is always intriguing. Probably one reason is that we know so little about them. It is an intrinsic trait of nature that is held by all animals, including the human animal, to express unusual interest in the mysterious or the unknown.

Dr. Ronchese has certainly given us much food for thought in his excellent review of nail anomalies and dystrophies. The late George Henry Fox was interested in the subject and was so engrossed in the anomalies of the nail plate that when a patient presented one, regardless of its nature, he recorded "disease of the nails" as a diagnosis on the patient's history.

When we learn more about nails we shall know more about hair. There are many respects—embryologic, anatomic and physiological—in which they are identical. In fact, the only important physiological difference is that growth of the nail plate is a continuous process whereas growth of hair is periodically interrupted.

Dr. Ronchese's remarks on the relation of transverse bands to arsenical intoxication and illness are well known. Here the analogy to hair is also evident. Arsenic can be found in the hair shaft as well as in the nail plate in cases of chronic arsenism. Temporary thinning of scalp hair is common in malaria, arsenism and Hodgkin's disease but as far as I know does not occur in psoriasis although trophic changes in the nails are common in that disease.

Transverse furrows also bear a direct relation to illness. Doubtless mental shock and psychodynamic trauma interfere with normal nail growth as they do with growth of hair. These types of trauma affect different persons in different ways. The metabolic activities of all persons do not react to identical environmental trauma in the same manner. The phlegmatic person and the stoic may manifest no nail changes.

That point brings us to the immediate cause of many of these trophic nail disorders. Excluding microbic invasion, contact onychia and congenital anomalies, all these changes must be due to nutritional deficiencies, since the nail plate consists of lifeless tissue. Protein deficiencies and lipid, calcium and sulfur deficiencies have been indicated. The changes associated with psoriasis, lichen planus, Darier's disease, senility, hypothyroidism, syphilis, Morvan's disease, diabetes, scleroderma, dermatomyositis, anesthetic leprosy and Raynaud's disease I think are all nutritional in origin, due indirectly to deficiencies of endocrine function.

Deficiencies of protein metabolism are particularly important. Tyson recently reported benefit in the cases of several women with fragile, splitting nails with longitudinal fissures after the administration of gelatin, 7 Gm. daily by mouth. Gelatin is not a complete protein food, since it lacks tyrosine, cystine and tryptophane. However, it is a scleroprotein containing most of the same amino acids as keratin. The same author reports benefit from the treatment in the case of a patient with psoriasis of the nails.

I am of the opinion that if Dr. Ronchese follows up his present interest in nails he will find that many changes associated with various toxemias arise, not directly because of the effect of some toxin on nail growth, but indirectly, through an effect of that toxin on hormonal function. The dramatic effect of ACTH in subacute disseminate lupus erythematosus, an infectious toxemia, is accomplished on this basis.

I wish again to congratulate Dr. Ronchese on his stimulating presentation.

DR. A. R. WOODBURNE, Denver: I want to make one comment about the transverse bands. I think that they are a not uncommon manifestation of dermatitis medicamentosa. I know that most of us who saw a great deal of quinacrine dermatitis saw frequent instances of canary yellow transverse bands of the nails in that condition.

DR. NELSON PAUL ANDERSON, Los Angeles: There are several comments I should like to make regarding Dr. Ronchese's paper. The short and wide thumb nail, the racket thumb nail, is in my experience rather uncommon. I have seen a few such thumb nails, which I called micronychia for want of a better term. If we examine the nails of all our patients we will find many interesting, unusual and rare nail conditions.

For years I have been trying to collect cases of syphilis involving the nails. I have been able to find only two cases that I could really classify as of syphilis involving the nails. I think the French school of dermatology in general has been very prone to overemphasize the role of syphilis in all disorders of unknown causation. Some of the nail conditions which Dr. Ronchese presented as the dystrophia mediana canaliformis of Heller are simply longitudinal grooving due to pressure on the nail bed by so-called traumatic epithelial cysts. One finds them in women who have had their nails manicured or in men after that trauma or other injuries at the base of the nail.

The other type of cyst which occurs at the base of the nail is the synovial cyst. I have one case of an epithelial cyst producing a longitudinal grooving of the nail in which bone formation developed. The few cases of true dystrophia mediana canaliformis of Heller which I have seen have responded to the removal of foci of infection, and such foci have been apical abscesses of teeth. As a matter of fact, one of these abscesses occurred in a dentist who was totally unaware of any trouble with his teeth.

There is another type of lateral nail dystrophy which Dr. Ronchese mentioned and which is the subject of a recent communication in the British literature. This condition primarily involves the thumb nails. Occasionally it affects the index finger. When it involves the thumb nail it usually involves the lateral side of the thumb nail and produces a hemidysplasia of both thumb nails. Associated with this condition are the concomitant observations of rudimentary or absent patellas and arthrodysplasia of the elbow joints. The patients have iliac horns which can be shown roentgenologically on the ilium and a severe renal dysplasia with many observations that might easily be mistaken for those of a chronic glomerular nephritis.

Occasionally small multiple angiomas of the skin are found. The whole syndrome is definitely hereditary and familial. In a recent British communication (Hawkins, C. F., and Smith, O. E.: Renal Dysplasia in a Family with Multiple Hereditary Abnormalities Including Iliac Horns, *Lancet* **1**:803 [April 29] 1950) it was related that a bitter family quarrel arose from doubts as to the paternity of a baby boy because the infant did not evidence the family abnormalities. I would like to say that Dr. Ronchese with his presentation of rare, unusual and unique dermatological conditions seems to be well on his way to becoming the F. Parkes Weber of American dermatology.

DR. F. RONCHESE, Providence, R. I.: I wish to thank the discussers, and particularly Dr. Anderson, for their kind remarks. From time to time it is proper to reevaluate signs and symptoms of diseases to check on their usefulness. In this reevaluation many claims have to be discarded and relegated to medical history. I regret that no new or better ideas resulted from this investigation. Dr. Combes mentioned ACTH. In a recent paper (Thorn, G. W., et al.: The Clinical Usefulness of ACTH and Cortisone, *New England J. Med.* **242**:783 [May 18] 1950) an illustration shows black transverse bands on the nails in a Negro treated for three weeks with a combination of cortisone and ACTH. It is an interesting observation, but only one, and it would be rather unwise to conclude from that one observation that ACTH and cortisone are the only causes of transverse pigmented bands on the nails.

INTERDIGITAL INFECTIOUS SYPHILITIC LESIONS SIMULATING DERMATOPHYTOSIS

Report of Ten Cases

HELEN TAYLOR DEXTER, M.D.
CINCINNATI

SYPHILIS is traditionally an infection which simulates the symptoms and physical observations of many other diseases. This paper reports a series of 10 cases in which the lesions of secondary syphilis resembled dermatophytosis of the feet. In two of these a local Herxheimer reaction occurred after the first therapeutic injection of penicillin.

T. L. Chin [1] in China in 1932 reported three cases with dermatophytosis-like syphilitic lesions. In 1940 Thomas and Bluefarb [2] described six similar cases in New York, and L. Selmi [3] found one such case in Italy in 1941. Stokes [4] and his associates mention a patient with interdigital syphilitic condylomata in their textbook. Undoubtedly this small number of cases is not indicative of the incidence of such lesions but perhaps of the failure to recognize their syphilitic etiology.

Of interest is the incidence of similar foot lesions in another systemic disease of spirochetal origin, yaws. Dr. Edouard Petrus [5] states that in Haiti interdigital lesions in early yaws are rare (0.5 to 1 per cent) even though the natives frequently go barefooted.

In two of our cases the systemic diagnosis of syphilis was made on the basis of interdigital lesions which on examination proved to be dark field positive; the diagnoses were further confirmed by high positive titers in the standard serologic tests. In the other eight cases generalized maculopapular lesions and condylomata lata of the genital areas were present and responsible for the original diagnosis of secondary syphilis; the foot lesions were observed and dark field examinations were performed to complete the work-up of the cases.

The cases are summarized in table 1.

From the Department of Dermatology and Syphilology of the College of Medicine of the University of Cincinnati, Dr. Leon Goldman, director.

1. Chin, T. L.: Syphilis of the Toes Resembling Fungus Infection (Hongkong Foot): Report of 3 Cases, Chinese M. J. **46**:60-63 (Jan.) 1932.

2. Thomas, E. W., and Bluefarb, S. M.: Early Syphilitic Lesions Mistaken for Dermatophytosis, Arch. Dermat. & Syph. **42**:11-14 (July) 1940.

3. Selmi, L.: Rare Interdigital Localization of Secondary Syphiloderma: Case, Boll. Soc. med. clin. Modena **42**:600-602, 1941-1942.

4. Stokes, J. H.; Beerman, H., and Ingraham, N. R., Jr.: Modern Clinical Syphilology: Diagnosis, Treatment, Case Study, ed. 3, Philadelphia, W. B. Saunders Company, 1944, p. 560.

5. Petrus, E.: Personal communication to the author.

TABLE 1.—*Data on Ten Cases of Interdigital Infectious Syphilitic Lesions*

Case No.	Patient	Month in Which Lesion Appeared	Results of Serologic Test for Syphilis and Fungus Culture	Foot Lesions	Other Lesions	Lymph Node Involvement	Local Herxheimer Reaction	Occupation
1*	H. P., white man aged 28	August	Serologic reaction positive; fungus culture negative	Cracked, ulcerative lesions between toes, both feet; foul-smelling discharge; dark field positive	Copper-colored lesions, palms and soles; crusted ulcerative lesions, pretibial areas	Inguinal, epitrochlear (bilateral)	+	Unemployed yard man
2*	J. A., Negro man aged 39	February	Serologic reaction positive	Sharply marginated lesions between fourth and fifth toes, right foot; dark field positive	Generalized papulopustular eruption; mucous patches in mouth	Generalized enlargement	+	Lumber yard man
3*	M. A., Negro woman aged 22	July	Serologic reaction positive; fungus culture negative	Ulcerative lesion beneath fourth toe, extending between the third and fourth toes	Papulopustular lesions on palms, soles, face and thighs; condyloma latum of labium	Axillary and inguinal (bilateral)	0	Domestic
4*	T. B., Negro woman aged 24	February	Serologic reaction positive	Soft friable ulcerative granulomatous lesions, fourth and fifth toes, left foot; foul-smelling; dark field positive	A few scattered erythematous macules on trunk; alopecia	Posterior cervical	0	Housewife
5	W. A., Negro man aged 28	June	Serologic reaction positive; (mucocutaneous relapse); fungus culture negative	Ulcerated condylomas between toes; hyperkeratotic ulcers on soles; dark field positive	Macules on palms and soles; papular lesion on prepuce; mucous patches on tonsils	Anterior cervical, bilateral inguinal	0	Laborer
6	E. C., Negro girl aged 19	January	Serologic reaction positive; fungus culture negative	Deep ulcerated fissure between first and second toes, right foot; condylomas between right fourth and fifth toes; dark field positive	Generalized erythematous papules	Epitrochlear and axillary (bilateral)	0	Housewife
7	M. A., white woman aged 23	December	Serologic reaction positive, 200 Kahn units	Erythematous ulcer; tissue maceration between first and second toes, left foot; cracks with maceration between other toes; dark field positive	Scaling, copper-colored macules on palms; condylomas in region of vulva and anus; maculopapular lesion on nostril, chin and lips; maculopapular lesions of scalp; alopecia	Cervical, axillary, inguinal	0	Household worker
8	P. F., white woman aged 23	December	Serologic reaction positive	Deep cracks between toes, both feet; condyloma latum type lesion between left third and fourth toes; dark field positive	Macules in palms	Left inguinal, cervical, axillary	0	Waitress
9	D. G., Negro woman aged 22	October	Serologic reaction positive	Erythematous ulcer between left fourth and fifth toes, 2 mm. deep; bloody, serous exudate; dark field positive	Hyperpigmented macules on both forearms; erosion of anterior lip of cervix	Left inguinal, epitrochlear	0	Unemployed
10	B. D., Negro girl aged 16	April	Serologic reaction positive; fungus culture negative	Ulcerated condyloma, medial side third toe; dark field positive	Perianal condylomas	Inguinal, axillary, epitrochlear, posterior and anterior cervical	0	Household worker

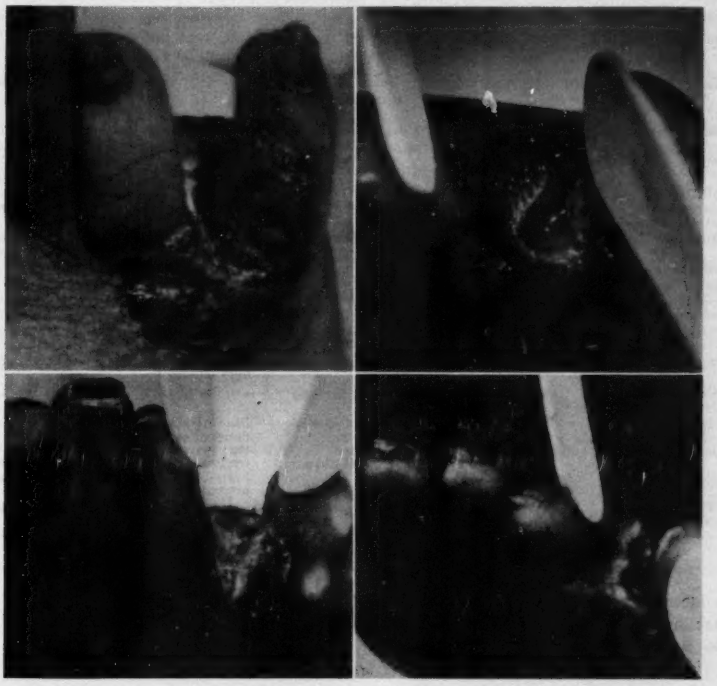
* Lesions in cases 1, 2, 3 and 4 are shown in the accompanying figure.

One case in which a Herxheimer reaction occurred will be described. The toe lesions seen in the patient are typical of those found in the other patients.

REPORT OF A CASE

H. D., a 27 year old white man, entered the Cincinnati General Hospital on Aug. 1, 1949.

History.—Two months preceding his admission the patient acquired an ulcerative penile lesion which disappeared within about four weeks on home treatment with saline soaks and a sulfonamide powder. One month before admission red spots began to appear on the palms and



Interdigital ulcers in secondary syphilis, cases 1, 2, 3, and 4.

soles and cracks developed between the toes of both feet. In spite of home remedies, the cracks became deeper and broader. On the patient's admission to the hospital these lesions were found to be dark field positive and the patient was treated. He had no history suggestive of previous attacks of epidermophytosis.

Physical Examination.—The abnormal observations in this patient were confined to his skin and lymphatic systems. The general texture and moisture of the skin were normal. On the palms and soles were numerous reddish brown macules about 6 mm. in diameter. A few crusted lesions about 1 to 3 cm. in diameter were scattered over the knees and pretibial areas. Extending from between the toes to the dorsal surface of the foot were deep cracks from which foul-smelling seropurulent discharge exuded; this discharge formed yellowish crusts. The lesions between the toes were ulcers about 1 cm. in diameter and 2 mm. deep. The craters were of equal depth over the entire surface. The bases were dark red and glistening after crusts were removed. Surrounding the craters were rims of macerated skin 2 to 5 mm. wide and elevated 1 to 2 mm.

above the surrounding skin. Although the lesions were indurated locally, there was little induration of the surrounding tissue and no evidence of cellulitis or lymphangitis. No scaling was present elsewhere on the foot. The inguinal and epitrochlear nodes were enlarged and nontender. No lesions were present on the genitalia.

Laboratory Examinations.—The lesions between the toes were dark field positive for Treponema pallidum. In the quantitative Kahn test the titer was 120 units. Cultures were negative for fungi. The white blood cell count was 7,000.

Hospital Course.—After the first injection of 33,333 units of aqueous penicillin, the patient complained of severe throbbing pain in his toes and the distal ends of the metatarsals. After the third injection of 33,333 units of penicillin (six hours later) the edema and erythema began to decrease, as did also the discharge from the interdigital lesions. Improvement was steady from that time. The ulcers epithelized both from the edges and from the craters. By the fifth day of treatment no discharge was present. On the patient's dismissal from the hospital on the tenth day after having received 2,400,000 units of penicillin (at that time the standard dose),

TABLE 2.—*Points in Differential Diagnosis of Syphilitic Interdigital Lesion and Epidermophytosis*

	Syphilitic Interdigital Lesions	Epidermophytosis
Organisms	Treponema pallidum	Fungi
Serologic reaction	Positive	Negative (or, if positive, coincidental)
History	Usually no previous foot lesions	Past episodes of epidermophytosis of the feet
Season of occurrence	Any season	Commoner in summer
Occupational environment	Any environment	Feet frequently hot or wet
Other lesions	Secondary syphilitic lesions elsewhere on skin and mucous membranes	Lesions confined to feet and possible id reactions on hands
Lymphatics	Generalized lymphadenopathy	Inguinal nodes on side involved only ones enlarged
Cellulitis and lymphangitis	Absent	Usually present
Characteristics of interdigital lesion	Ulcerative lesion, sharply demarcated; crater uniformly deep, shiny, and dark in color; rim of macerated tissue but general area around ulcer not involved	Ulcerative lesion more eroded than punched out; base uneven and dull red; macerated epidermal tissue extending irregularly several millimeters beyond border of ulcer and sometimes present in patches in the ulcer
Therapeutic response	Response to penicillin; no response to local therapy	Response to local therapy; no response to penicillin unless some secondary infection associated (occasional id type of penicillin reaction)

the ulcers were almost entirely epithelized and the cracks had closed. No local therapy was administered. The crusted lesions on the legs were healed, and the macules on the palms and soles had faded.

COMMENT

The foregoing case is interesting in that the interdigital lesions were dark field positive and responded to penicillin antisyphilitic therapy first with a localized Herxheimer reaction and then with rapid healing. The interdigital lesions in all the cases epithelized and disappeared rapidly after penicillin therapy without any topical medication.

It is important to establish the criteria for syphilis in the differential diagnosis of interdigital lesions. Of course, other skin and mucous membrane lesions of a syphilitic type and a positive serological reaction for syphilis with a high titer are significant observations. As yet we have not encountered a dark field positive lesion in a seronegative patient, and none has been reported.

The course and appearance of the interdigital involvement is somewhat different in syphilis and dermatophytosis. In the latter there has usually been chronic scaling and cracking of the skin on the feet and between the toes preceding the onset of

the ulceration. An explanation of the development of the severer lesions can frequently be found in a history of exposure of the feet to excessive heat or moisture. The rare case of epidermophytosis with ulcers as extensive as those found in syphilis is accompanied with more edema, erythema and induration of the surrounding tissues. Cellulitis and lymphangitis usually are present. The ulcers of epidermophytosis are less sharply demarcated, shallower and more irregular in depth; the appearance is that of spotty superficial erosion. The bases are less red. Evidence of scaling and maceration of adjacent tissue is usually found. Lymphadenopathy, if present, is limited to the inguinal nodes of the involved side in contrast to the more generalized lymph node enlargement which is usually present in secondary syphilis.

In the cases seen in this hospital no seasonal incidence of interdigital syphilitic lesions is evident. The patients did not have occupations which would cause their feet to be either hot or abnormally moist. Most of the patients denied previous attacks of any but minimal epidermophytosis. In five of the cases fungus cultures were made, all of which were negative.

SUMMARY

Ten cases are reported of interdigital secondary syphilis of the feet that simulated the lesions of epidermophytosis. Some of the lesions were condylomas, but most were ulcerative forms.

One case in which a Herxheimer reaction of the foot lesions occurred is described in detail.

The points of possible differential diagnosis are discussed.

DEVELOPMENT OF BASAL CELL EPITHELIOMA AS A CONSEQUENCE OF RADIODERMATITIS

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AND
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SHORTLY after Roentgen discovered the rays which bear his name there appeared reports in the medical literature regarding the development of carcinoma as a consequence of radiodermatitis. With rare exceptions these reports have brought out a thought which has become almost accepted as a fact, namely, that such carcinomas are always prickle cell in type. It is the purpose of this paper to show that such carcinomas are not invariably of the prickle cell variety. In doing this we will summarize a few reports from the literature and report a number of cases in which the ensuing carcinomas were basal cell in character.

HISTORICAL DATA

Wilhelm Conrad Roentgen discovered "X rays" in November 1895 and announced his findings through the Physical-Medical Society of Würzburg in December of that year. Almost immediately there were reports of erythema, dermatitis and deep ulceration from the use of these rays. In 1896 Marcuse [1] reported alopecia and a dermatitis resembling a sunburn from the use of roentgen rays. Other early reports regarding the effects of these rays on the skin came from Gilchrist [2] in 1897, Kienböck [3] in 1900, Codman [4] in 1902, Halkin [5] in 1903 and Unna [6] in 1904. Codman noted that the worst cases presented a slough and possessed a tendency to undergo malignant change.

Read before the Section on Dermatology and Syphilology of the California State Medical Association, San Diego, April 29, 1950.

1. Marcuse, W.: Nachtrag zu dem Fall von Dermatitis und Alopecie nach Durchleuchtungsversuchen mit Röntgenstrahlen, Deutsche med. Wchnschr. **22**:481 (July 23) 1896.

2. Gilchrist, T. C.: Cases of Dermatitis Due to the X-Rays, Bull. Johns Hopkins Hosp. **8**:17 (Feb.) 1897; Additional Cases of Dermatitis Due to the X-Rays, ibid. **8**:46 (March) 1897.

3. Kienböck, R.: Ueber die Einwirkung des Röntgen-Lichtes auf die Haut, Wien. klin. Wchnschr. **13**:1153 (Dec. 13) 1900.

4. Codman, E. A.: A Study of the Cases of Accidental X-Ray Burns Hitherto Recorded, Philadelphia M. J. **9**:438 (March 8) and 499 (March 15) 1902.

5. Halkin, H.: Über den Einfluss der Becquerilstrahlen auf die Haut, Arch. f. Dermat. u. Syph. **65**:201, 1903.

6. Unna, P. G.: Die chronische Röntgendermatitis der Radiologen, Fortschr. a. d. Geb. d. Röntgenstrahlen **8**:67, 1904.

Haagensen [7] and Silverstone [8] credited Frieben as being the first to announce a case of carcinoma caused by roentgen rays. Frieben's report appeared in 1902 and concerned the case of a maker of x-ray tubes. Ledoux-Lebard [9] cited Lindenborn as having reported 29 cases of roentgen ray tumors in 1906 and also noted that Kassabian in 1907 reported seven deaths from roentgen ray cancer. Porter and White [10] accumulated a series of 10 cases of prickle cell cancer on the hands of physicians. In 1909 Rowntree [11] presented a report from England of 11 cases of roentgen ray cancer. Porter [12] in the same year reported a series of 47 similar cases from the United States. Wolbach [13] in presenting a histological study of Porter's cases stated that of the 47 lesions 36 were epidermoid carcinomas and two were questionable sarcomas. In 1922 Rowntree,[14] as he stated in a follow-up article on three further cases, believed the smaller number of cases which he reported then meant that physicians were using better protection from radiation. At that time he stated that cancer developed in practically all cases of roentgen-ray dermatitis from 1899 to 1906. In 1921 MacKee and Andrews [15] compared the reactions of the skin to roentgen rays and to radium and found no essential difference. H. N. Cole [16] in 1924 believed that roentgen ray dermatoses in physicians and technicians were far more numerous than the literature would lead one to believe. Ochsner [17] presented the case of a physician with many believed keratoses, and Leddy and Rigos [18] compiled data on 39 other cases in physicians, stating that the damage from roentgen rays was caused by ignorance and carelessness.

The passage of time brought forth many additional articles which inclined toward the belief that all or practically all carcinomatous degenerations following radiodermatitis were prickle cell in nature. MacNeal and Willis [19] in 1923 reported the case of a squamous cell carcinoma on the right thumb of a physician which developed after repeated exposures to radium. Pfahler [20] stated that as far as

7. Haagensen, C. D.: Occupational Neoplastic Disease, Am. J. Cancer **15**:641 (April) 1931.

8. Silverstone, S. M.: Radiation Cancer, J. Mt. Sinai Hosp. **9**:74 (July-Aug.) 1942.

9. Ledoux-Lebard, R.: Le cancer des radiologistes, Paris méd. **12**:299 (April 8) 1922.

10. Porter, C. A., and White, C. J.: Multiple Carcinomata Following Chronic X-Ray Dermatitis, Ann. Surg. **46**:649 (Nov.) 1907.

11. Rowntree, C. W.: X-Ray Carcinoma, Brit. M. J. **2**:863 (Sept. 25) 1909.

12. Porter, C. A.: The Surgical Treatment of X-Ray Carcinoma and Other Severe X-Ray Lesions, Based upon an Analysis of 47 Cases, J. M. Research **21**:357 (Sept.) 1909.

13. Wolbach, S. B.: The Pathological Histology of Chronic X-Ray Dermatitis and Early X-Ray Carcinoma, J. M. Research **21**:415 (Oct.) 1909; Summary of Effects of Repeated Roentgen-Ray Exposures upon Human Skin, Antecedent to Formation of Carcinoma, Am. J. Roentgenol. **13**:139 (Feb.) 1925.

14. Rowntree, C. W.: X-Ray Cancer, Brit. M. J. **2**:1111 (Dec. 9) 1922.

15. MacKee, G. M., and Andrews, G. C.: Roentgen Dermatitis and Radium Dermatitis: A Comparison, Arch. Dermat. & Syph. **4**:213 (Aug.) 1921.

16. Cole, H. N.: Chronic Roentgen-Ray Dermatoses as Seen in the Professional Man, J. A. M. A. **84**:865 (March 21) 1925.

17. Ochsner, E. H.: X-Ray Carcinoma of Both Hands, Am. J. Surg. **28**:273 (May) 1935.

18. Leddy, E. T., and Rigos, F. J.: Radiodermatitis Among Physicians, Am. J. Roentgenol. **45**:696 (May) 1941.

19. MacNeal, W. J., and Willis, G. S.: A Skin Cancer Following Exposure to Radium, J. A. M. A. **80**:466 (Feb. 17) 1923.

20. Pfahler, G. E.: Electrocoagulation or Desiccation in the Treatment of Keratoses and Malignant Degeneration which Follow Radiodermatitis, Am. J. Roentgenol. **13**:41 (Jan.) 1925.

he knew the malignant changes were always of the squamous cell type and therefore serious. Irradiation accounted for 30 per cent of carcinomas of the hand, and all but a very few were squamous cell in type, according to Mason.[21] Cancer arising in chronic radiodermatitis was stated by Michael [22] to be practically always of the spinocellular variety. Haagensen [7] reported 17 cases of squamous cell carcinomas, two of osteogenic sarcomas and one of lymphatic leukemia among cases of malignant disease caused by roentgen rays, radium and radioactive substances while Finzi [23] spoke of the great tendency for epitheliomas to develop in chronic radiodermatitis. Handley [24] recorded several cases of squamous cell carcinoma of the hand in radiologists and recommended complete dissection of the axillary glands as part of the surgical treatment.

One of the most complete studies was that of Saunders and Montgomery,[25] who in 1938 analyzed 259 cases of chronic roentgen ray and radium dermatitis in which 27 epitheliomas developed. These were all of the squamous cell type. At this time Saunders and Montgomery stated that more of these lesions were due to therapeutic exposure than were due, as in former years, to occupational exposure. The next year Duffy [26] agreed by saying nearly all the pathological reports on such cases revealed either fibrocarcinoma or squamous cell carcinoma. Daland [27] followed with the statement that roentgen ray cancer was usually of the epidermoid type, and Silverstone,[8] with the statement that the commonest type was that of squamous cell carcinoma which behaved like the spontaneously occurring variety. Reports of cases of squamous cell epithelioma in roentgen ray dermatitis were added by Phillips [28] and by Curtis.[29]

Recent textbooks present similar opinions. H. Montgomery, in the text (p. 287) of MacKee and Cipollaro,[30] stated that epitheliomas arising from areas of radiodermatitis, whether from keratoses or ulcers, are of the squamous cell type, that he had never seen a true sarcoma arising from chronic radiodermatitis and finally that "it is questionable whether basal cell epithelioma ever results from radiodermatitis; its occasional association probably is merely coincidental." MacKee himself, however, was less dogmatic and in the same text [31] stated that

21. Mason, M. L.: Carcinoma of the Hand, Arch. Surg. **18**:2107 (May) 1929.

22. Michael, J. C.: The Pathology of Radiodermatitis, Texas State J. Med. **26**:710 (Feb.) 1931.

23. Finzi, N. S.: Late X-Ray and Radium Effects: Incidence, Etiology, and Medical Treatment, Brit. J. Radiol. **6**:148 (March) 1933.

24. Handley, W. S.: The Treatment of X-Ray Carcinoma and X-Ray Dermatitis, Lancet **1**:120 (Jan. 20) 1934. Improved Outlook in X-Ray Carcinoma, Lancet **1**:1122 (June 22) 1940.

25. Saunders, T. S., and Montgomery, H.: Chronic Roentgen and Radium Dermatitis, J. A. M. A. **110**:23 (Jan. 1) 1938.

26. Duffy, J. J.: Irradiation Keratosis and Carcinoma, Am. J. Roentgenol. **42**:540 (Oct.) 1939.

27. Daland, E. M.: Radiation Damage to Tissue and Its Repair, Surg., Gynec. & Obst. **72**: 372 (Feb.) 1941.

28. Phillips, C.: Observations Based Upon the Studies of 1,434 Skin Cancers, Virginia M. Monthly **67**:400 (July) 1940.

29. Curtis, G. H.: Radiodermatitis: Its Prevention as Sequel to Roentgen Therapy for Certain Common Dermatoses, Cleveland Clin. Quart. **9**:3 (Jan.) 1942.

30. MacKee, G. M., and Cipollaro, A. C.: X-Rays and Radium in the Treatment of Diseases of the Skin, ed. 4, Philadelphia, Lea & Febiger, 1946, p. 287.

31. MacKee and Cipollaro,[30] p. 240.

"Baso-squamous and occasionally pure basal cell tumors develop in chronic radiodermatitis." Citing the article of Saunders and Montgomery [25] Sutton and Sutton [32] note that such epitheliomas are always squamous cell in type. Ormsby and Montgomery [33] stated in discussing radiodermatitis that the "epitheliomas are usually squamous cell in character and rarely are of basal cell type." Similar statements are made by MacKee and Cipollaro [34] and Roxburgh.[35]

REPORT OF CASES

Case 1.—A woman aged 37 presented a chronic moderately severe radiodermatitis of both sides of the face. This occurred 16 years after she had received four or five treatments by the Tricho method for the removal of superfluous hair. She was advised to use vitamin A and D ointment locally. Nearly four years later she returned with a large, dime-sized, elevated, firm, waxy-appearing tumor located exactly at the tip of the chin. This measured 1.2 by 1.4 cm. with a height of 6 to 7 mm. This lesion was removed by electrosurgery. Biopsy revealed a definite basal cell epithelioma of the adenoid variety.

Case 2.—W. F. M., aged 37 years, had received an unknown amount of roentgen radiation from five different physicians for an eczematous condition of the face. On examination definite and characteristic changes of radiodermatitis were present over most of the face as well as on the vermilion border of the lower lip. In addition typical basal cell epitheliomas were present in the left malar region and on the columella of the nose. Both lesions were removed by means of electrosurgical procedures and studied microscopically. Each lesion proved to belong in the basal cell epithelioma group. The basal cells tended to be of spindle cell shape.

Case 3 (data furnished by Dr. J. Walter Wilson).—The patient was a 31 year old white woman who gave a history of having had severe acne in her adolescence which had been treated once a week with roentgen radiation for three months at a "clinic" which is no longer in operation. It has not been possible to ascertain the total dose of roentgen radiation. During the succeeding years atrophic scarring developed in a number of areas on the forehead and cheeks with some telangiectasia. Several years ago a small protuberance appeared in the center of one of these scarred areas in the region of the left malar eminence. Within the past three months this lesion had increased to perhaps double its size.

The patient presented a 6 mm. semiglobular, waxy, translucent nodule clinically suggestive of basal cell epithelioma. The lesion was removed *in toto*, with the use of a procaine hydrochloride block, by means of a curet, and the base was desiccated thoroughly. Histopathological examination revealed a structure typical of basal cell epithelioma.

Seven additional similar cases have been observed. Their histories would simply be repetitions of the above. It is to be noted that in each instance there was microscopic confirmation of the diagnosis of basal cell epithelioma. The location of the lesions observed in the total 10 cases is given in the accompanying figure. It will be noted that the great majority of the lesions occurred either in the exact midline of the face, e. g., forehead, alae nasi, columella of the nose or the tip of the chin, or in the vicinity of the malar regions. These areas are those subject to "overlapping" in roentgen ray treatments or in which, as with the malar regions, an error in distance measurement would cause considerable increase in the delivered roentgen dose (inverse square law).

32. Sutton, R. L., and Sutton, R. L., Jr.: Diseases of the Skin, ed. 10, St. Louis, C. V. Mosby Company, 1939, p. 190.

33. Ormsby, O. S., and Montgomery, H.: Diseases of the Skin, ed. 7, Philadelphia, Lea & Febiger, 1948, p. 253.

34. MacKee, G. M., and Cipollaro, A. C.: Cutaneous Cancer and Precancer: A Practical Monograph, New York, American Journal of Cancer, 1937, p. 69.

35. Roxburgh, A. C.: Common Skin Diseases (General Practice Series), ed. 8, Philadelphia, The Blakiston Company, 1948, p. 86.

CASE 11.—J. H., a 67 year old retired white man who had formerly been a bathhouse attendant, was first examined in November 1948 complaining of "x-ray burns" on his arms and back. He stated that 22 years previously, in Buffalo, New York, he had worked as a bathhouse attendant and that it had been necessary for him to wear a bathing suit type of costume. He had had considerable hair on his arms and upper part of the back which had had to be shaved frequently so that he would look presentable. Because of this situation he had Tricho treatments to destroy this unwanted hair. Eight years after the treatments he noticed depigmentation of the skin, and 20 years after therapy (two years before his examination by us) he noted that lumps were appearing in the areas of depigmentation.

Examination of the skin revealed depigmentation, telangiectasia, atrophy and small and large indurated nodular lesions on the outer aspect of each arm from the shoulder to the elbow and

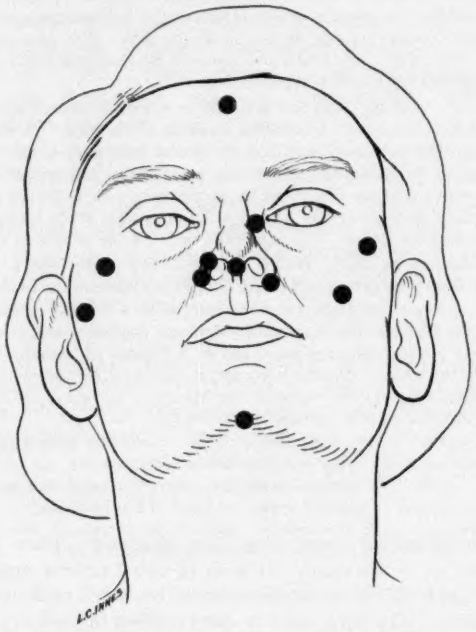

Diagram of the face showing the location of basal cell epitheliomas occurring in 10 patients whose skin was damaged by roentgen rays. (One patient [case 3] had two lesions.)

a hand-sized area on the midline of the upper part of the back. There were about eight nodular lesions on the right arm and about 25 nodular lesions on the left arm. There were six superficial type epitheliomas on the neck and lateral aspects of the chest which were not in the areas of radiation damage. The clinical diagnosis was chronic radiodermatitis with malignant degeneration.

A large nodular lesion 1.5 cm. in diameter was excised with the use of local anesthesia and a specimen sent for biopsy. The section showed a rather atrophic epidermis except in areas where there were buds of proliferating large basal cells. There were also many large and small nests of these large basal cells scattered throughout the cutis and surrounded by a heavy fibrous tissue stroma. These nests of basal cells had a "glandlike" appearance. The superficial vessels were dilated, and the dermal glands were atrophied. The diagnosis was basal cell epitheliomatous degeneration in chronic radiodermatitis.

Most of the nodular lesions were destroyed by electrodesiccation with the use of local anesthesia without recurrence.

In our opinion case 11 is somewhat analogous to the case of Scharnagel and Pack.[36] Our patient had superficial epitheliomatosis which developed in both irradiated and nonirradiated areas years after his radiation injuries had occurred. Those in the normal or nonirradiated skin remained as typical lesions of superficial epitheliomatosis. Those which developed in the areas injured by irradiation took on an elevated fungating appearance, and their histological appearance was that of adenoid basal cell epitheliomas as contrasted with the multicentric picture presented by those lesions in normal skin.

REFERENCES TO BASAL CELL EPITHELIOMA FOLLOWING RADIODERMATITIS

Searching the literature one finds a reference as early as 1927 regarding basal cell carcinomas attributed to the influence of roentgen rays. O'Donovan's[37] patient, a professional radiographer, presented 15 such lesions, but his case cannot be accepted as presented. In 1928 Burrows[38] recorded a case of basal cell carcinoma of the scalp appearing 18 years after epilation by roentgen rays for ringworm. In 1936 Tod[39] stated that basal cell carcinoma and sarcoma had been described but said that these had arisen in roentgen ray scars and that the causal relationship was not definitely established. More recently Warren[40] stated he had seen basal cell carcinoma develop on the basis of radiation injury. Cannon,[41] in a biopsy study of the last 11 neoplasms which formed in a roentgen ray burn, found that eight were basal cell epitheliomas; two were squamous cell, and one, basosquamous cell. Andrews[42] has recorded a case in which he excised 47 small basal cell epitheliomas with five to eight new lesions developing every three or four months. This situation occurred 11 years after roentgen ray therapy for acne. Also of interest is that the patient had practically no more lesions after treatment with injection of crude liver extract given twice weekly.

Studying the local effects of radioactive phosphorus (P_{32}) beta rays on rats, Henshaw, Snider and Riley[43] found a tendency to the formation of both squamous cell and basal cell carcinoma as well as fibrosarcoma and presented photomicro-

36. Scharnagel, I. M., and Pack, G. T.: Multiple Basal-Cell Epithelioma in a Five Year Old Child, Am. J. Dis. Child. **77**:647 (May) 1949.

37. O'Donovan, W. J.: Multiple X-Ray Basal-Celled Carcinomata of the Trunk, Proc. Roy. Soc. Med. (Sect. Dermat.) **21**:17 (Dec.) 1927.

38. Burrows, H.: Basal-Celled Carcinoma of Scalp Appearing 18 Years After Epilation by X-Ray for Ringworm, Brit. J. Radiol. **1**:59 (Feb.) 1928.

39. Tod, M. C.: X-Ray and Radium Injuries of the Skin and Mucous Membranes, Lancet **2**:755 (Sept. 26) 1936.

40. Warren, S.: Effects of Radiation on Normal Tissues: XIII. Effects on the Skin, Arch. Path. **35**:340 (Feb.) 1943; The Histopathology of Radiation Lesions, Physiol. Rev. **24**:225 (April) 1944.

41. Cannon, A. B.: Skin Tumors, Bull. New York Acad. Med. **23**:163 (March) 1947.

42. Andrews, G. C.: Possible Prevention of Cancer in Chronic Radiodermatitis by Medical Means, Connecticut M. J. **13**:105 (Feb.) 1949.

43. Henshaw, P. S.; Snider, R. S., and Riley, E. F.: Aberrant Tissue Developments in Rats Exposed to Beta Rays: The Late Effects of P_{32} Beta Rays, Radiology **52**:401 (March) 1949.

graphs which were quite typical of these conditions. Shafer and associates [44] reported the cases of 35 patients with roentgen injuries on the face, 20 of whom had epitheliomas. They made biopsies of the tumors in 16 patients and found that in 11 single or multiple basal cell epitheliomas occurred either as the only microscopic observation of neoplasm or in association with other lesions of the squamous cell type. In their summary of the histological observations three squamous cell epitheliomas, two basosquamous cell epitheliomas, four basal cell epitheliomas and basosquamous or squamous cell epitheliomas and seven single or multiple basal cell epitheliomas were mentioned. They went on to state that

> the occurrence of basal cell epitheliomas in radiodermatitis does not appear to be coincidental. In this series neoplasms developed in persons of a younger age group than is ordinarily reported. Furthermore, they occurred more than twice as frequently among women as among men, which is the reverse of the usual observation. These facts suggest that the basal cell epitheliomas in these patients were, in most instances, associated with and related to the presence of the chronic radiodermatitis.

An interesting case is that of a 5 year old child studied by Scharnagel and Pack,[36] who had been given roentgen ray therapy for an enlarged thymus. Later the child manifested over 1,000 nodular lesions, mostly in the irradiated area, which clinically were diagnosed as papillary pigmented nevi but which on repeated biopsy study proved to be basal cell epitheliomas of the hair matrix type. Further, Macleod and Muende [45] stated that the keratoses and superficial ulcers in "x-ray dermatitis are liable to develop into carcinomata of the basal-cell type." Andrews [46] summarized the subject well by saying that "whereas the usual growth is an infiltrating squamous carcinoma, basal-cell carcinoma, sarcomas and malignant melanomas have been observed in both human beings and animals." Cannon,[47] in discussing a case of Bechet's, stated, "Most epitheliomas occurring in roentgen ray burns are of the basal cell variety. My statistics show nine basal cell lesions to every squamous cell epithelioma. The more pronounced and deeper the radiation burn and the larger the growth, the more likely the epithelioma is to be the squamous cell variety." Traub,[47] in discussing the same case, stated that very often basal cell lesions develop in areas of radiodermatitis, probably even more frequently than do prickle cell lesions. He thought that it was "probably commoner for one to see basal cell forms in areas of mild dermatitis, and prickle cell lesions where the radiodermatitis has been severe."

MacKee and Cipollaro,[48] in a follow-up of cases of folliculitis ulerythematosa reticulata, made note of the presence of chronic radiodermatitis in their case 2. Associated with this were three basal cell epitheliomas situated as follows: in the center of the right cheek, on the side of the nose and near the outer aspect of the

44. Shafer, J. C.; Braestrup, C. B., and Fisher, J. K.: Relation of Exit Dose and Other Dosage Factors to Roentgen Injuries, Arch. Dermat. & Syph. **59**:472 (April) 1949.

45. Macleod, J. M. H., and Muende, I.: Practical Handbok of the Pathology of the Skin: An Introduction to the Histology, Pathology, Bacteriology, and Mycology of the Skin with Special Reference to Technique, ed. 2, New York, Paul B Hoeber, Inc., 1940, p. 108.

46. Andrews, G. C.: Diseases of the Skin for Practitioners and Students, ed. 3, Philadelphia, W. B. Saunders Company, 1946, p. 73.

47. In discussion on Bechet, P. E.: Radiodermatitis with Multiple Epitheliomas, Arch. Dermat. & Syph. **61**:344 (Feb.) 1950.

48. MacKee, G. M., and Cipollaro, A. C.: Folliculitis Ulerythematosa Reticulata, Arch. Dermat. & Syph. **57**:281 (March, pt. 1) 1948.

left eyebrow. These lesions were excised, and the "histologic structure was that of basal cell epithelioma and chronic radiodermatitis." They went on to state that "basal cell epitheliomas in chronic radiodermatitis are not uncommon but the consensus at present is that such lesions are not sequelae of radiodermatitis but that they would have developed anyway."

COMMENTS

One of the neglected facts in dealing with the sequelae of roentgen radiation is that such sequelae depend a great deal on the tissue which has been damaged. Thus one would never expect to find any lesion except a prickle cell epithelioma arising from roentgen injury of the palms and soles. Basal cell epitheliomas, as far as one can determine, have never been observed in such areas. A similar situation exists with regard to the sequelae of radiodermatitis involving mucous membranes, such as the lip, buccal, vaginal and anal mucosa. Similarly the great majority of prickle cell epitheliomas develop in radiodermatitis involving the dorsum of the hand. This is an area in which the development of basal cell carcinoma is very rare, although it does occur. Sachs and Garbe [49] reported eight instances of basal cell epitheliomas of the hand among 32 cases of primary basal cell epithelioma of the extremities.

In other words, skin damaged by roentgen rays can react only by the development of prickle cell or basal cell epithelioma—or, rarely, fibrosarcoma or, with extreme rarity, malignant melanoma (Andrews [46]). Carcinoma of the lung and pleura may follow roentgen damage to the chest contents. Bone damaged by roentgen rays can respond only by the development of either fibrosarcoma or osteogenic sarcoma. Repeated injury of the blood-forming organs (bone marrow) can give rise only to aplastic anemia, lymphatic or myelogenous leukemia or some similar variant. This last-mentioned observation is well demonstrated by the mortality tables of dermatologists, roentgenologists and radiologists.

The objection will be raised that histological proof is lacking of the actual development of basal cell epithelioma in an area of radiodermatitis. This is undoubtedly true except for the three lesions in case 2 of MacKee and Cipollaro.[48] These were removed by excision and did show "a histologic structure of basal cell epithelioma and chronic radiodermatitis." MacKee and Cipollaro regarded the development of these epitheliomas as coincidental. In most cases, however, the situation is similar to that which existed in our series. All the lesions were removed by electrosurgical procedures after sufficient tissue for microscopic studies had first been secured by means of a punch or a curet. The criticism that there was a failure to make a histological confirmation of radiodermatitis in such cases may with equal justice be extended to many, although not all, the reports dealing with the development of prickle cell epitheliomas subsequent to radiodermatitis.

The clinical observations which have been made by Michelson, Torrey, J. W. Wilson, Cannon, Traub, Andrews, Shafer and ourselves are not to be ignored simply because someone has written that the development we record cannot take place. Future observations and investigations of the ideas expressed in this paper will bear out their truth.

49. Sachs, W., and Garbe, W.: Primary Basal Cell Epithelioma of the Extremities, Arch. Dermat. & Syph. **36**:273 (Aug.) 1937.

Lever's [50] proposition that basal cell epitheliomas are nevoid tumors (hamartomas) was based on two premises. Lever's first premise was, "Basal cell epitheliomas cannot be produced experimentally. Experimentally produced carcinomas of the skin always are squamous cell epitheliomas."

One can only point to the experimental work of Henshaw and co-workers [43] which was published a year later than Lever's work. These workers noted that a great variety of aberrant tissues developed in the skin of rats after the local application of P_{32}. The lesions produced were basal cell epitheliomas, prickle cell epitheliomas and spindle cell sarcomas. There was no correlation of particular tumor types with types or dosage of exposure. Also to be noted was the fact "that tissue could be caused to elaborate one kind of abnormal growth and immediately adjacent to this to form another type of growth or remain quiescent." It is true that P_{32} produces beta radiation, but it is our understanding that, according to the present theories of the action of roentgen rays, the final or ultimate effect of roentgen rays on the cell is the result of beta radiation (particles).

From the clinical aspect the history of arsenic exposure or ingestion together with the presence of arsenical keratoses of the palms and/or soles in the great majority of cases of superficial epitheliomatosis would seem to raise serious doubts as to the correctness of Lever's first premise. There have been innumerable case presentations and reports confirming the role of arsenic as an etiological agent in many of the cases of superficial epitheliomatosis since the work of one of us in 1932.[51]

Also from the clinical aspect, basal cell epitheliomas on rare occasions have been noted after exposure to pitch, tar and asphalt (Hueper [52]). Incidentally, Hueper also gives five separate references to the development of basal cell epithelioma or intermediate types occurring in roentgen-damaged skin [53]; only one of the works cited was available and has already been cited (O'Donovan [37]).

Lever's second premise in the proposition that basal cell epitheliomas are nevoid tumors was that "basal cell epitheliomas may occur in large number, widely distributed over the skin, without provocation by a carcinogenic agent." That this statement is partly true is shown by the three cases cited. It was the privilege of one of us (N. P. A.) to observe personally on several occasions one of these cases (Nisbet's). However, for Lever to include multiple basal cell epitheliomas of the trunk and extremities in the same category as the cases of Nomland and Nisbet is not in accordance with the overwhelming clinical evidence of arsenical causation in many cases of superficial epitheliomatosis. Not too much is known regarding carcinogenic agents, but certainly roentgen rays and arsenic are among them.

It is undoubtedly true that nevoid rests of basal cell type occur in the skin and may be stimulated to further development by various means. That such a sequence

50. Lever, W. F.: Pathogenesis of Benign Tumors of Cutaneous Appendages and of Basal Cell Epithelioma: II. Basal Cell Epithelioma, Arch. Dermat. & Syph. **57**:709 (April) 1948.

51. Anderson, N. P.: Bowen's Precancerous Dermatosis and Multiple Benign Superficial Epithelioma: Evidence of Arsenic as an Etiologic Agent, Arch. Dermat. & Syph. **26**:1052 (Dec.) 1932.

52. Hueper, W. C.: Occupational Tumors and Allied Diseases, Springfield, Ill., Charles C Thomas, Publisher, 1942, p. 108.

53. Hueper,[52] p. 266.

occurred in the case of Scharnagel and Pack [36] already cited would seem reasonable. In our case 11, which is somewhat analogous to that of Scharnagel and Pack, a similar development took place in the areas of radiodermatitis although several lesions of superficial epitheliomatosis developed in areas which showed no sign of roentgen damage.

Dr. Frances Torrey [54] has told us of an instance of widespread radiodermatitis of the extremities following the use of roentgen rays for the removal of hair. In this case multiple epitheliomas developed in the areas damaged by radiation. A number of these were prickle cell in type, but also a considerable number were basal cell in character. The former seemed to develop in the areas most severely damaged by roentgen radiation. It would seem foolish to ascribe the prickle cell lesions to the sequelae of radiation and to say that the basal cell lesions were coincidental or were a happenstance or occurred because of nevoid rests.

An analogous situation occurs in the well defined disease xeroderma pigmentosum, in which malignant changes of various types occur. The commonest lesion is that of basal cell epithelioma, but prickle cell epitheliomas, malignant melanomas, sarcomas and endotheliomas may occur.[33] To ascribe the basal cell epitheliomas in xeroderma pigmentosum to one group and the prickle cell epitheliomas, melanomas, sarcomas and endotheliomas to one or more separate groups does not appear logical.

With regard to lesions on the face, where such nevoid embryonic basal cell rests are said to exist in the vicinity of the embryonic facial fissures, it is not so easy to ignore Lever's idea. It would be simple to assume in our cases of radiodermatitis involving the face that the roentgen rays or some other agent, such as the actinic rays, had stimulated such a nevoid rest into activity.

However, as was pointed out by Shafer and co-workers [44] in their discussion on the relation of the exit dose to radiation injuries, the radiodermatitis occurring on the face developed after repeated exposures over long periods. Furthermore, the skin changes tended chiefly to involve the middle portion of the face, with the nose, lips and chin presenting the most decided changes. In addition to the high exit dose produced by roentgen radiation to the sides of the face, there are the additional factors of excessive radiation, overlapping of the fields and possible midface exposure technic.

One can readily see from the figure that in general the distribution of the basal cell epitheliomas in our cases is considerably different from that of the lesions which arise spontaneously.

THERAPY

The logical therapy of basal cell epitheliomas which develop in areas of roentgen ray damage would seem to include surgical excision. This, however, is not always practical, and removal of such lesions by the actual cautery or by electrosurgical methods may be done according to the preference of the physician. In all cases the diagnosis should be confirmed by biopsy. It is our considered opinion that neither roentgen rays nor radium has any place in the treatment of such lesions.

From a prophylactic standpoint some factors to be considered include the administration of liver extract two or three times weekly as advocated by Andrews. Protection from sunlight, the use of emollients, the administration of large doses

54. Torrey, F.: Personal communication to the authors.

of vitamin A and perhaps the local use of vitamin A and D-containing ointments are additional procedures which might be worthy of trial. Cannon[55] speaks highly of the value of electrodesiccation in the treatment of roentgen-damaged skin.

CONCLUSIONS

Basal cell carcinomas may develop in cutaneous areas which have been damaged by roentgen rays or radium.

Basal cell epitheliomas do not develop as a sequel to radiation injuries of the palms, soles or mucous membranes.

Many, if not most, basal cell epitheliomas which develop in areas of skin damaged by roentgen ray radiation are most probably the direct result of such injury and are not merely coincidental.

ADDENDUM

Since this paper was submitted for publication the following articles have appeared. These may be of additional interest on this subject.

Blom-Ides, C.: Sarcoma in Röntgenoderma, Acta dermat.-venereol. **30**:47, 1950.

Mutscheller, A.: The Biological Significance of the Roentgen, J. Invest. Dermat. **14**:471 (June) 1950.

Stewart, C. B., and Pendergast, W. J.: Fibrosarcoma Developing in Heavily Irradiated Skin, J. M. A. Georgia **40**:24 (Jan.) 1951.

Eckhoff, N. L.: Recurrent Multiple and Metastasizing Basal-Celled Carcinomata, Brit. J. Plast. Surg. **3**:264 (Jan.) 1951.

2007 Wilshire Boulevard, Los Angeles (Dr. N. P. Anderson).

501 Post Building, Battle Creek (Dr. H. E. Anderson).

55. Cannon, A. B.: The Treatment of X-Ray Burns and Other Superficial Disfigurements, New York State J. Med. **40**:391 (March 15) 1940.

TREATMENT OF CUTANEOUS TUBERCULOSIS WITH LOCAL INJECTIONS OF STREPTOMYCIN

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ONE OF the problems in the dermatological field has been the treatment of cutaneous tuberculosis, cure being rare. Recently, however, the apparent cure of this condition in remarkably short periods has been achieved by infusion of streptomycin, intracaine® (beta-diethylaminoethyl para-ethoxy benzoate) hydrochloride and epinephrine into tuberculous lesions and surrounding areas of the skin. I have found that in this manner streptomycin can be used much more effectively and without the side effects encountered with other parenteral methods. The treatment leaves little scar tissue, does not require maintenance of streptomycin levels and can be carried out in the office. The primary aim of this report is twofold: (1) to demonstrate a practical method whereby cutaneous tuberculosis may be healed clinically and (2) to formulate rational, consistent attitudes and approaches to the problem of tuberculosis of the skin.

FACTORS IN STREPTOMYCIN THERAPY

In order to determine the dose, duration of treatment and method of administration of streptomycin, certain factors have to be considered, such as the objectives, the therapeutic possibilities and the limitations of the drug as well as methods of increasing permeability of the cells and maintaining the concentration of the drug in situ.

It is well known that patients with skin tuberculosis rarely have active tuberculosis of the pulmonary type; therefore, it would seem logical that local therapy would be sufficient to care for isolated tuberculous lesions of the skin. Infusion at the site of the lesion increases the accessibility of the solution of streptomycin to the tubercle organisms. The actual physical penetration of the streptomycin into the active area of tuberculous involvement is necessary to accomplish this purpose. Proliferative and fibrocaseous tubercles are readily penetrated by a variety of substances, such as local anesthetics, dyes and the sulfones. Streptomycin appears to be freely distributed throughout the extracellular fluid of the body as well as all viable inflammatory tissue. The distribution of intracellular and extracellular bacilli, because it affects both the intensity of the infection, whether acute or chronic, and the vulnerability of the organisms to the drug, is an important factor in determining the effectiveness of the streptomycin at the site of the inoculum. Little is known concerning proportions of intracellular and extracellular organisms in the various types of tuberculous lesions. It is thought that in the actively proliferating tubercles there is a predominance of extracellular organisms whereas in chronic quiescent tubercles the organisms tend to become intracellular, especially in the

monocytes. As some of the bacilli are found in the monocytes, it is unknown whether or not they are reached by the streptomycin. Some investigators feel that the streptomycin surrounds the monocytes and other cells, forming a film about the cell membrane. The extracellular organisms, however, would be easily accessible to the streptomycin.

Streptomycin therapy of skin tuberculosis in the past has been limited to parenteral use with unsatisfactory results. It has been briefly alluded to by several authors; no cases have been reported and no results tabulated. The only reference to local streptomycin injection was by Wolfer, Hirshliefer and Shapiro,[1] who employed local infusion with parenteral therapy in one case of tuberculous ulcer of the tongue and came to the conclusion that it was of no value. The dosage used by these authors was 0.1 Gm. daily for 15 days.

REASON FOR GIVING INTRACUTANEOUS INJECTIONS

The concentration of streptomycin in the skin appears to be very low with the usual dose given parenterally. Furthermore, Leopold and Nichols[2] found that low concentrations did not appear in the cornea before two hours and then only when a dose of 100,000 units per kilogram was given. Since the absorption of the streptomycin was so infinitesimal on the cornea when the drug was given by parenteral injections, some other method of administration was deemed advisable. The amount necessary parenterally to produce an effective concentration in the skin would be so great that with its use serious complications, such as eighth nerve involvement, deafness or sensitivity to the drug, would certainly develop. The effective use of streptomycin in the treatment of cutaneous tuberculosis requires (1) that the concentration be high enough for the drug to act both as a bactericide and as a bacteriostatic agent and (2) that the drug act on the intracellular as well as extracellular tubercle organisms. Normally the parenteral injection of streptomycin cannot raise the concentration enough to create a bactericidal action. However, when the drug is infused directly into the tissue involved there is an overwhelming concentration in a localized area, permitting the necessary bactericidal and bacteriostatic action.

It would appear that the danger of the development of resistant strains is lessened when the lesions of tuberculosis are treated adequately the first time. If the concentration of streptomycin used in the treatment does not suppress completely the multiplication of the organisms, variant tubercular bacilli may arise which are streptomycin resistant and as a result are able to multiply until eventually they constitute a preponderance of the infecting organisms. For all practical purposes the physician gets only one chance with streptomycin in the treatment of tuberculosis because of the formation of these resistant strains. The bactericidal action of streptomycin varies directly with the concentrations, both in vivo and in vitro, provided that the organism has not become resistant to the drug through previous contact. Streptomycin appears to have an inhibiting action on the reproduction of the bacterial cell, that is, the rate of increase, and the number of bacteria begins to decrease at a certain concentration of streptomycin and continues to decrease as

1. Wolfer, H.; Hirshleifer, I., and Shapiro, R.: Treatment of Tuberculous Ulcer of Tongue with Streptomycin, J. A. M. A. **136**:249-250 (Jan. 24) 1948.

2. Leopold, I. H., and Nichols, A.: Intraocular Penetration of Streptomycin Following Systemic and Local Administration, Arch. Ophth. **35**:33-38 (Jan.) 1946.

the concentration of the streptomycin is increased. The individual cell sensitivity to the drug varies; therefore, the most sensitive cells would be affected first. As the concentration of the drug increases eventually all the tubercle bacilli would be inhibited from completing their cycle of cell division and the whole process of generation and regeneration would be blocked. Streptomycin appears to have both bacteriostatic and bactericidal action to a great extent, depending on the time of contact, the organism involved, the concentration of streptomycin and the size of the area. Other factors are also significant, such as the pH, the temperature and the state of activity of the lesion—that is, whether it is arrested or is actively progressing. Tubercle bacilli do not produce an antagonist to streptomycin. Streptomycin is not destroyed in their presence, nor is a significant amount of streptomycin removed from the medium during growth. Berkman, Henry and Housewright [3] found that they were able to recover 30 to 60 per cent of streptomycin from the urine. The rapid excretion of streptomycin in the urine caused my associates and me to add epinephrine to our solution in order to maintain a high concentration of streptomycin in the area. The irritating and hemorrhagic properties of the streptomycin were also lessened by the addition of epinephrine to the solution.

Abraham and Duthie [4] have found that streptomycin activity is extremely sensitive to the concentration of salt in the environment. The addition of 2 per cent salt may increase the minimal inhibiting concentration of streptomycin 100 times. There appears to be no satisfactory explanation for the antagonistic effect of salt on streptomycin. In view of this effect, it would seem advisable to keep the blood chlorides low during the infusion period.

PROCEDURE USED

Because of the extreme pain produced by streptomycin dissolved in distilled water when injected by infusion into the diseased skin area, a 2 per cent solution of intracaine® was used as a diluent. This procedure allowed me and my associates to infuse a concentrated solution of streptomycin into the involved area without pain or other untoward effect. The dose depends on the size of the infected area, the advisability of maintaining as high a concentration as possible being kept in mind. One gram of streptomycin will dissolve into 1 cc. of intracaine® and epinephrine, 1 : 1,000, producing a nearly concentrated solution with a bulk of 1.75 cc. and a pH of 4.3. We did not use over 1 Gm. daily in any of the cases presented although we feel it would be perfectly safe to give 2 Gm. daily in this manner if the affected area is large enough to justify the use of this amount. The method of administration of streptomycin, intracaine® and epinephrine was by intradermal infusion, with blanching of the epidermis but without production of a bleb. This can be done with very little pain to the patient if the injection is started slowly with slight pressure applied to the syringe. A slight burning sensation, probably due to the low pH of this concentration, is noticed at the very beginning of the injection. Pain on injection of streptomycin was a serious problem until the drug was dissolved in intracaine.®

3. Berkman, S.; Henry, R. J., and Housewright, R. D.: Studies on Streptomycin: Factors Influencing Activity of Streptomycin, J. Bact. **53**:567-574 (May) 1947.

4. Abraham, E. P., and Duthie, E. S.: Effect of pH of Medium on Activity of Streptomycin and Penicillin and Other Chemotherapeutic Substances, Lancet **250**:455-459 (March 30) 1946.

REPORT OF CASES

Following is a résumé of three cases of cutaneous tuberculosis treated by infusion of streptomycin, intracaine® and epinephrine into the active lesions.

CASE 1.—F. P., a 24 year old Mexican, when first seen by me was apparently well except for extensive vegetative plaques varying from the size of a dime to that of a silver dollar. These plaques were erythematous, indurated and indolent and presented multiple minute

Fig. 1 (case 1).—Lesions before treatment with streptomycin, intracaine® and epinephrine.

pustules throughout the active areas which encircled the entire left hand and wrist. The area emitted a foul, putrid odor. The patient stated he had had the eruption since childhood. Once or twice each year it would flare up for a few months and then become quiescent. It had not disappeared at any time. The patient had a job washing dishes at the time of the present flare-up, which had begun about a month before he sought my advice. He had had no previous treatment for the condition. The hand had always been a hindrance to him, keeping him from employment.

The family history was rather vague. Both parents had died of unknown causes. The patient had been reared by relatives whose health was questionable.

Clinical laboratory reports were as follows: Wassermann reaction, negative; results of routine urinalysis, essentially normal; red blood cells, 4,900,000; white blood cells, 8,700; hemoglobin, 97 per cent; Schilling's shift to the left, 1:11:0; polymorphonuclear leukocytes, 60 (segmented neutrophils, 55; staff cells [stabs], 5; lymphocytes, 33; monocytes, 5, and eosinophils, 2.

Roentgenologic examination of the chest revealed no demonstrable pulmonary or cardiac pathological features. Smears made from a piece of tissue stained for tubercle bacilli were negative. Guinea pig inoculation from the same piece of tissue was positive for tubercle bacilli.

Fig. 2 (case 1).—Lesions after treatment with streptomycin, intracaine® and epinephrine.

Culture for tubercle bacilli showed typical colonies of the organisms. Culture for fungi was negative. Graduated old tuberculin intradermal tests were given which gave the following reactions: 1:10, 4+; 1:100, 2+, and 1:1,000, 2+. A patch test for tuberculosis elicited 1+ reaction.

Histopathological Report.—A section from the skin of the left wrist showed an atrophic epidermis covered by a hyperkeratotic stratum corneum. In some areas intraepidermal abscesses were seen. The epidermal pegs were elongated and irregular and extended into the papillary portion of the cutis which in places had been replaced by nodules of epithelioid cells and surrounding mantles of lymphocytes. Above these nodules in the papillary bodies one

could see congested, dilated capillaries. The Ziehl-Neelsen stain for acid-fast organisms was negative. The diagnosis was tuberculosis verrucosa cutis. (The slide was reviewed by Dr. Louis Winer.)

Treatment.—The patient received 46.4 Gm. of streptomycin in a 2 per cent solution of intracaine® with a 1 : 1,000 dilution of epinephrine injected intracutaneously in 54 divided doses between March 11 and May 17, 1949. On May 17, at which time the photograph in figure 2 was taken, the hand was apparently clear of all lesions and the skin was normal except for considerable depigmentation. At the time of this writing, the hand appeared normal.

CASE 2.—T. F., a Japanese woman aged 23, first noticed a hard lump on her left cheek at the age of 12 years. Other lesions gradually appeared on her face and the lateral aspects of both upper arms, the neck and the back. In 1942 the patient consulted a physician, who

Fig. 3 (case 2).—Lesions before treatment with streptomycin, intracaine® and epinephrine.

"burned" the lesion and removed several brown kernels. The lesion soon returned to its initial condition. At her first visit to our office she presented three separate areas of involvement: the lower part of the left cheek, the center of the right cheek and the right temple, neck, back and outer aspect of both arms. The lesions were erythematous and deeply indurated with reddish brown, multiple nodules throughout. Under diascopic pressure the inherent brown color of the individual nodules, commonly known as apple jelly nodules, could be seen clearly.

Histopathological Report.—In a section from the skin of the right jaw, the epidermis was atrophic and thin and raised from the cutis during the preparation of the slide. The stratum corneum was absent. In the lower part of the cutis was a dense nest of epithelioid cells, which in turn was surrounded by a mantle of lymphocytes. This lymphocytic infiltrate was seen to surround the vessels in the entire cutis. The Ziehl-Neelsen stain for acid-fast organisms was negative. The diagnosis was lupus vulgaris.

In a section from the skin of the back the epidermis had a thin layer of stratum corneum which in places was parakeratotic. The rete was disintegrating in areas where the epidermal cells could be seen to be vacuolated. Beneath this zone of degenerated epidermis, the papillary part of the cutis was washed out and edematous. The upper and middle reticular parts of the cutis contained a nodule with caseation necrosis, epithelioid cells, Langhans' giant cells and a peripheral zone of lymphocytes. The Ziehl-Neelsen stain for acid-fast organisms was negative. The diagnosis was lupus vulgaris.

(Both slides were reviewed by Dr. Louis Winer.)

Routine examination of the blood and urine gave normal results. Serologic reactions were negative. Roentgenologic examination of the chest was negative for tuberculosis.

Fig. 4 (case 2).—Lesions after treatment with streptomycin, intracaine® and epinephrine.

Treatment.—The patient was given 30 injections of streptomycin, with a 2 per cent solution of intracaine® and a 1 : 1,000 dilution of epinephrine (total 28.5 Gm.), into the lesions intracutaneously. When the patient was seen on March 21, 1950, the lesions had completely disappeared.

CASE 3.—L. T., a white woman aged 46, had had an eruption on the right ear since 5 years of age. Since that time she had noted puffing and indurated areas of the ear which would occur and later partially disappear. Each time the size of the affected area appeared to increase slightly. The condition finally progressed until papular induration involved the entire ear. In August 1949, while cutting her hair, the barber accidentally traumatized the ear and the area seemed to bleed profusely.

When first examined the patient presented erythematous, indurated, brownish papular lesions involving the entire outer part of the helix of the right ear. Diascopic examination revealed typical apple jelly nodules.

A roentgenologic examination of the chest revealed no observations of pathological significance. A blood count taken October 4 showed white blood cells, 6,700; red blood cells, 4,230,000, with hemoglobin, 76 per cent; polymorphonuclear leukocytes, 54 (segmented neutrophils, 49; staff cells [stabs], 5); lymphocytes, 41; large monocytes, 4, and eosinophils, 1, with a sedimentation rate of 34 mm. per minute and a platelet count of 207,270. The serologic reaction was negative.

Histopathological Report.—In a section from the skin of the right ear the epidermis was atrophic and compressed from below. The papillary part of the cutis was condensed and had a slight cellular infiltrate. In the upper and middle reticular portions of the cutis were several definite nodules consisting of central nests of epithelioid cells with an occasional giant cell and surrounded by dense mantles of small lymphocytes. One nodule, rather superficial had caseation necrosis in its center. Surrounding this necrosis was a zone of epithelioid cells, the periphery of which contained several giant cells. The Ziehl-Neelsen stain for acid-fast organisms was negative. The diagnosis was lupus vulgaris of the tumidus type. (The slide was reviewed by Dr. Maximilian Obermayer and Dr. Louis Winer.)

Treatment.—The patient received 21 injections of streptomycin, 500 mg. dissolved in 0.5 cc. of a 2 per cent solution of intracaine® with epinephrine, 1:1,000. This solution was diffused into the entire outer part of the helix of the right ear. On several occasions the reaction was severe and was allowed to subside before continuance of the injections. When the patient was last seen, on April 24, 1950, the ear appeared entirely normal.

COMMENT

The dosage of streptomycin varies with the size of the lesion and the area involved. We have tentatively employed 1 Gm. daily for approximately 20 days; however, in the case of the ear lesion described in case 3, because of the smaller area involved, we used approximately 0.5 Gm. daily with apparently equally satisfactory results. The duration of treatment was decided purely on an empirical basis, and no optimum time has been determined. In one of our cases 38 days of treatment were required; in another, 45 days, and in the remaining case, 54 days. Injections were given daily except where the induration and hemorrhagic bullae precluded further injections until these manifestations were resolved. We believe that because of the overwhelming concentration of streptomycin no resistant strains were developed. If the entire lesion cannot be covered in a few injections, it is advisable to cover as large an area as possible in the first injection and to continue the following day where the previous injection terminated, taking all precautions to make injections well into the junctions.

The local reaction frequently results in a hemorrhagic bulla which if not disturbed will remain intact until a hard crust forms, this cycle being completed in approximately 10 days. It must be emphasized here that the injections should be continued until there is no visible lesion. Whether further injections should be made after the crust has been removed depends on the appearance of the epidermis at the site.

It is impossible to evaluate the clinical therapeutic possibilities of streptomycin infusion in dermatological conditions without the knowledge gained from treatment of an adequate number of subjects over a period sufficiently long for one to judge properly the curative powers of the drug. It is obvious that no final conclusions can be justifiably drawn from the results of the treatment of three patients, but definite curative trends are apparent.

It is hoped that the information given in this paper will stimulate others to further study, that controls will be instituted and a definite program established whereby it will be proved whether the antibiotic or the chemotherapeutic action

of the streptomycin is the curative factor. Considerable thought was given to the possibility of running a control in the cases herein described by using inactivated streptomycin but the measure was rejected because we were afraid that the inactivated streptomycin might produce a resistant strain of tubercle bacilli which would preclude a cure later with the active drug.

EVALUATION

Clinical evidence of the efficacy of streptomycin, intracaine® and epinephrine infusion in the treatment of tuberculosis of the skin is far from conclusive, but results to date have been dramatic. The enthusiasms of the initial success should not blind us to the potentialities for even well arrested tuberculosis to relapse. It is well known that tuberculosis which is clinically healed may be undergoing a latent period of inactivity. We should recognize that bacilli may persist for years after the disease appears inactive clinically and be on guard against the danger of premature and erroneous conclusions concerning the lasting effects of streptomycin infusion therapy.

SUMMARY AND CONCLUSIONS

Three cases of tuberculosis of the skin were treated by infusion with streptomycin, intracaine® and epinephrine with apparent cures.

I am unable to state whether the cure was effected by the antibiotic action of the drug or by its chemotherapeutic action.

Experimental use of streptomycin therapy in human subjects is a hazardous procedure because of the danger of producing resistant strains of tubercle bacilli.

Proof of the success of this treatment will depend on the results obtained by many other clinicians over a period of years.

TREATMENT OF TINEA CAPITIS WITH A NEW ANTIFUNGAL COMPOUND

Preliminary Report

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AND
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DURING the past few years various antifungal agents were introduced for the treatment of tinea capitis, especially the anthropophilic [1] type caused by Microsporum audouini. Conflicting results have been reported, with cure rates varying from 10 to 100 per cent.[2] In general, the time required for cure has been six or more months of arduous, meticulous treatment. As a consequence, many physicians resorted to x-ray epilation, which unquestionably is the most rapid method of therapy today. However, the obvious advantages of topical treatment of tinea capitis have impelled the members of the medical profession to continue their search for an antifungal agent which is distinguished by low toxicity, a low sensitizing index, rapid effectiveness and ease of application and which would be cosmetically acceptable to the patient. The present report deals with results attending the use of a new antifungal compound which more nearly approximates having

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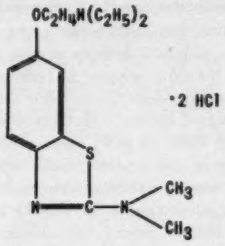
1. Wise, F., and Sulzberger, M. B.: The 1938 Year Book of Dermatology and Syphilology, The Year Book Publishers, Inc., Chicago, 1939, p. 31.

2. (*a*) MacKee, G. M.; Hermann, F., and Karp, F. L.: New Treatment for Anthropophilic Tinea Tonsurans (Microsporon Audouini), J. Invest. Dermat. **7**:43-52 (Feb.) 1946. (*b*) Carrick, L.: Methods of Local Therapy for Tinea Capitis Due to Microsporon Audouini, J. A. M. A. **131**:1189-1194 (Aug. 10) 1946. (*c*) Schwartz, L.; Peck, S. M.; Botvinick, I.; Liebovitz, A. L., and Frasier, E. S.: Control of Ringworm of Scalp Among School Children in Hagerstown, Md., 1944-1945, J. A. M. A. **132**:58-62 (Sept. 14) 1946. (*d*) Lewis, G. M.; Hopper, M. E., and Reiss, F.: Ringworm of the Scalp: Clinical Data on Recent Cases; Experiences with Local Endocrine Therapy, J. A. M. A. **132**:62-65 (Sept.14) 1946. (*e*) Strickler, A.: Tinea Capitis: Its Treatment with Special Iodine and Dilute Acetic Acid, J. A. M. A. **132**:65-66 (Sept. 14) 1946. (*f*) Miller, J. L.; Lowenfish, P. F., and Beattie, G. F.: Local Treatment of Tinea Capitis, J. A. M. A. **132**:67-70 (Sept. 14) 1946. (*g*) Steves, R. J., and Lynch, F. W.: Ringworm of the Scalp: Report of Present Epidemic, J. A. M. A. **133**:306-309 (Feb. 1) 1947. (*h*) Combes, F. C.; Zuckerman, R., and Bobroff, A.: Copper Undecylenate in Treatment of Dermatomycoses, J. Invest. Dermat. **10**:447-453 (June) 1948. (*i*) Rees, R. B.: Treatment of Superficial Fungous Infections in Routine Dermatologic Practice, California Med. **69**:28-31 (July) 1948.

these properties than any substance we have previously employed in the treatment of tinea capitis. The paper is offered chiefly for the purpose of stimulating among other workers more widespread interest in the drug employed.

This preparation is chemically the dihydrochloride of 2-dimethylamino-6-(beta-diethylaminoethoxy) benzothiazole, having the following structural formula:



The compound was supplied by the manufacturers as a 2 per cent tincture in 70 per cent alcohol and as a 2 per cent ointment in carbowax® 1500. These materials

TABLE 1.—*Distribution of Offending Organisms in Seventy-Seven Patients with Tinea Capitis*

Offending Organisms	Total No. of Patients	No. of Patients with No Previous X-Ray Therapy	No. of Patients with Previous X-Ray Therapy
M. audouini	56 (73%)	44	12
M. lanosum	21 (27%)	20	1
Totals	77	64	13

were provided initially under the experimental code designation Ro2-2453 and later under the name of asterol® dihydrochloride.[3] The $L.D._{50}$ of the drug is 350 mg. per kilogram by subcutaneous administration to mice. In vitro experiments revealed inhibition of growth of M. audouini in a concentration of 1:160,000. This observation indicates that Ro2-2453 has several times greater activity in this respect than does undecylenic acid.

When prophetic patch tests with a solution, an ointment and a dusting powder, all containing 2 per cent Ro2-2453, were made on 200 subjects not requiring antifungal therapy there was no evidence of primary irritation. Similarly, none of these same 200 subjects showed a positive reaction on retesting two weeks later. This result indicates that Ro2-2453 is not a powerful sensitizer.

CASE MATERIAL AND METHOD OF TREATMENT

Ro2-2453 was employed in treatment of 84 patients with tinea capitis. There were 63 boys and 21 girls, ranging in age from 3 to 12 years. Seven patients were lost from observation. Thus, the number of adequately treated patients was 77. Sixty-four had not had x-ray therapy, and 13 had. The clinical diagnosis was verified by the presence of bright green fluorescence under Wood's light. Cultures of pathogenic fungi were obtained in all instances. As is seen from table 1, in 56

3. Supplies of the preparation were provided by Hoffmann-La Roche, Inc., of Nutley, N. J.

cases, or 73 per cent, the infection was caused by M. audouini, and in 21 cases, or 27 per cent, by Microsporum lanosum. It is our impression that during the past year there has been a higher incidence of tinea capitis caused by M. lanosum than in previous years.

The following regimen was employed: The hair was clipped short initially and subsequently every 7 to 10 days. The scalp was shampooed every other day with soft soap liniment (tincture of green soap). Ro2-2453 tincture was sprayed over the entire scalp every morning and rubbed in with an old toothbrush with soft bristles moistened with the liquid. The ointment was applied with a toothbrush in the same manner at bedtime. White, tight-fitting skull caps, made of muslin or other smooth cotton cloth, were worn constantly, day and night, and these were boiled after each 24-hour period of use. Mothers were instructed to remove manually obviously infected hairs, to collect them in paper bags and to burn them. Once a week all patients returned to the clinics or to our private offices, where their progress was evaluated under Wood's light and further manual epilation performed for at least five minutes in each case.[4] Six consecutive weekly negative results on Wood's light examination were arbitrarily chosen as our criterion of cure, but no patient was discharged from observation until three monthly examinations thereafter proved the absence of reinfection. In most cases treatment was discontinued after the third Wood's light examination which revealed no fluorescence.

TABLE 2.—*Results of Treatment with Ro2-2453 in Sixty-Four Patients with Tinea Capitis Having Had No Previous X-Ray Treatment*

Offending Organisms	No. of Patients	No. Whose Condition Became Wood's Light-Negative	No. Whose Condition Improved (Diminution of Fluorescence)	No. Showing Failure
M. audouini	44	32 (73%)	9 (20%)	3 (7%)
M. lanosum	20	14 (70%)	6 (30%)	0
Totals	64	46 (72%)	15 (23%)	3 (5%)

RESULTS

In three of the 12 cases due to M. audouini in which there had been x-ray treatment that therapy had failed. In these the results of Wood's light examination became negative after three to six weeks' treatment with Ro2-2453. In all the other cases in this group the condition was cured, but, of course, the results cannot be attributed to the antifungal compound. The group which had had no previous x-ray therapy is of particular interest. As is seen in table 2, in 32, or 73 per cent, of the 44 cases due to M. audouini and in 14, or 70 per cent, of the 20 cases caused by M. lanosum the results of Wood's light examination came to be negative after treatment with Ro2-2453. Thus, out of a group of 64 patients who had had no previous x-ray treatment, a total of 46, or 72 per cent, came to show no fluorescence on Wood's light examination.

In addition, 15 patients, or 23 per cent, were having improvement in their condition as evidenced by diminished fluorescence and a reduction in the number of Wood's light-positive hairs. Only three patients, or 5 per cent, of the 64 who had had no previous x-ray therapy showed no improvement. It is noteworthy that these patients, whose infection was due to M. audouini, did not cooperate in performing manual epilation at home. Similarly they did not permit adequate manual epilation in the clinic.

4. Wilson, J. F.: Manual Epilation in Treatment of Tinea Capitis, Arch. Dermat. & Syph. **60**:347-355 (Sept.) 1949.

The time required for the results of Wood's light examination to become negative after initiation of therapy with asterol® dihydrochloride and the period of follow-up which these patients had had to the time of writing are recorded in table 3.

As may be seen from this table, three to six weeks of treatment were required in 11 instances, or about ¼ of the cases, before the first negative result on Wood's light examination was obtained. In 30 instances, or approximately two thirds of the cases, six to 12 weeks were required for the first negative result of Wood's light examination, with the rest requiring less than three or over 12 weeks of treatment. As appears also from table 3, 22 of the 46 patients had six consecutive negative results of Wood's light examinations and 24 patients were reexamined less than five times.

In the total number of 56 cases due to M. audouini (this figure includes those that had had previous x-ray treatment) 19 patients, or 34 per cent,

TABLE 3.—*Time Required for First Negative Result on Wood's Light Examination and Period of Weekly Examinations of Forty-Six Patients with Tinea Capitis Rendered Wood's Light Negative with Ro2-2453*

	No. of Patients and Time Required for First Negative Result on Wood's Light Examination After Initiation of Treatment with Ro2-2453					No. of Patients Rendered Wood's Light Negative and Period of Weekly Examinations to Date	
Offending Organisms	1 Week	2 Weeks	3-6 Weeks	6-12 Weeks	12-16 Weeks	1-5 Weeks	6 or More Weeks
M. audouini	1	1	7	21	2	19	13
M. lanosum	..	1	4	9	..	5	9
Totals	1	2	11	30	2	24	22
Grand Totals	46					46	

acquired kerion during treatment with asterol® dihydrochloride. Of these, 17, or 90 per cent, came to have negative results on Wood's light examination within one to 12 weeks. When kerion occurred, treatment with the alcoholic tincture was found too irritating, and the patients who acquired it continued treatment with the ointment alone applied twice daily with gentle massage by the finger tips.

COMMENT

Tinea capitis has always posed quite a problem in our clinics. In the past we used other drugs, including those of the undecylenic acid or copper undecylenate type,[2h] those containing salicylanilide [2c] and others,[2a] conjointly with the same general measures employed in the present study. However, none of the previous drugs proved as effective as Ro2-2453. The truth of that statement is made evident not only by the comparative speed with which negative Wood's light observations were attained but also by the fact that it has not been necessary to resort to x-ray epilation in a single case since the use of this preparation was instituted. The three patients classified as showing treatment failure have not been treated by x-ray epilation since it is hoped that better results will be obtained with better cooperation.

The need for painstaking, diligent manual epilation, both by the dermatologist and by the parent, as an essential adjunct to treatment cannot be overemphasized. This point has recently been stressed by Wilson.[4]

Even with the possibility that one or more of the 24 patients who had had their hair rendered Wood's light negative and then had had weekly reexaminations for only one to five weeks might have a relapse before the sixth Wood's light examination, results were most gratifying. In fact, more patients may come to have negative Wood's light observations as treatment of the improved cases continues, thus increasing the number of those freed of the infection.

The incidence of kerion in the series presented is noteworthy, as is the high rate of negative Wood's light observations in patients after the development of kerion. In the past we have seen comparatively few cases of kerion in tinea capitis caused by M. audouini and treated by other topical agents, although we are aware that many such cases have been reported.[5] As has been noted by other observers,[5] infected hairs are spontaneously shed with the onset of a sharp inflammatory reaction and the patient goes on to a relatively rapid cure. The inflammatory reaction evidently renders the soil less favorable for the growth of the parasite. While this reaction might have been spontaneous, it might also have been directly attributable to the action of the antifungal agent. Studies are in progress to clarify this problem.

SUMMARY AND CONCLUSIONS

Seventy-seven patients with tinea capitis were treated with a new antifungal agent, asterol® dihydrochloride. Of the 13 patients who had had previous x-ray therapy, three showed failure of that therapy. These were cured after three to six weeks' treatment with asterol® dihydrochloride. In the 64 patients who had not had previous x-ray therapy, 44 cases were caused by M. audouini and 20 by M. lanosum. Seventy-three per cent of the former and 70 per cent of the latter were rendered Wood's light negative chiefly in three to 12 weeks, with an occasional case requiring as little as one or as much as 16 weeks of treatment. It has not become necessary to use x-ray epilation in a single case since we began the use of the new antifungal compound.

Since previous results with other antifungal preparations have been far less striking, it is concluded that Ro2-2453 is the most effective topical agent for the treatment of tinea capitis we have employed to date.

ADDENDUM.—In the light of the recent studies of Kligman and Anderson,[6] which were not available to us at the time our report was written, our observations may require reevaluation. This is in progress and will be included in a subsequent paper with follow-up studies.

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88-56 One Hundred and Sixty-third Street (Dr. Fishman).

88-29 One Hundred and Sixty-third Street (Dr. Laurens).

Dr. Leo A. Pirk gave valuable assistance throughout the course of this work.

5. Scully, J. P.; Livingood, C. S., and Pillsbury, D. M.: Local Treatment of Tinea Capitis Due to Microsporon Audouini: Importance of Inflammatory Reaction as Index of Curability, J. Invest. Dermat. **10**:111-118 (March) 1948.

6. Kligman, A. M., and Anderson, W. W.: Evaluation of Current Methods for the Local Treatment of Tinea Capitis, J. Invest. Dermat. **16**:155-168 (March) 1951.

DERMATITIS WITH LIPOMELANOTIC RETICULAR HYPERPLASIA OF LYMPH NODES

Report of Fifteen Cases

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THE ASSOCIATION of a peculiar type of hyperplasia of lymph nodes with chronic dermatitis was first fully discussed by Pautrier and Woringer [1] in 1937. They reported 11 cases in which the lymph nodes on histological examination showed a peculiar type of hyperplasia. The dermatitis varied in type and degree but was usually erythematous, desquamative, of localized distribution and associated with pruritus. The lymph node hyperplasia was characterized by the multiplication of reticular cells, the presence of intracellular fat and melanin pigment and slight infiltration with eosinophils. In 1941 Soloff [2] reported a case in which there were similar changes in the inguinal lymph nodes in a patient who died of disseminated miliary tuberculosis. In 1942 Hurwitt [3] reviewed 12 cases in which there occurred generalized lymphadenopathy in association with a variety of chronic skin disorders characterized by pruritus. Clinically the cases were suspected of being possibly in the lymphoblastoma group, Hodgkin's disease, mycosis fungoides or lymphosarcoma. Proper analysis of the histological features of the granulomatous character of the lymph nodes pointed in all cases to a benign, reactive process. That a progressive lymph node disease was absent was substantiated by prolonged follow-up observation. It should be noted that in many of the reported cases there was widespread lymphadenopathy, which fact led to a clinical diagnosis of lymphoblastoma.

Read before the Section on Dermatology and Syphilology at the Ninety-Ninth Annual Session of the American Medical Association, San Francisco, June 29, 1950.

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1. Pautrier, L. M., and Woringer, F.: Contribution à l'étude de l'histo-physiologie cutanée: à propos d'un aspect histopathologique nouveau du ganglion lymphatique; la réticulose lipomélanique accompagnant certaines dermatoses généralisées; les échanges entre la peau et le ganglion, Ann. dermat. et syph. **8**:256-273, 1937.

2. Soloff, L. A.: Lipomelanotic Reticular Hyperplasia of Lymph Nodes: Report of a Case, J. Lab. & Clin. Med. **27**:343-346, 1941.

3. Hurwitt, E.: Dermatopathic Lymphadenitis: Focal Granulomatous Lymphadenitis Associated with Chronic Generalized Skin Disorders, J. Invest. Dermat. **5**:197-204, 1942.

In a previous paper six cases of chronic dermatitis, pruritus and lymphadenopathy were recorded in 1948 by one of us (T. C. L.[4]), and the gross and microscopic features of lipomelanotic reticular hyperplasia of lymph nodes were described. In the present paper all these cases are now briefly discussed and their present status reviewed. In addition, nine other cases are reported with additional general and specific observations.

REPORT OF CASES

CASE 1.—A white woman aged 33 had had since adolescence a generalized disease of the skin which had been diagnosed as "neurodermatitis." On Nov. 10, 1949 pain, tingling and a small lump were noted in the right axilla. Examination showed a dry, scaling patchy eruption on the trunk and extremities with a moderately enlarged nontender right axillary lymph node. The hemoglobin was 12 Gm.; the red blood cell count was 4,800,000, and the white cell count was 5,350 with a normal differential count.

On Dec. 19, 1949 a slightly enlarged, otherwise not unusual axillary lymph node was removed. It showed the characteristic microscopic features of lipomelanotic reticular hyperplasia.

This patient was last seen March 1, 1950. Tingling and itching of the skin were still present on many occasions. The appearance of the skin was as previously noted, and no palpable enlarged lymph nodes were present.

CASE 2.—A white girl aged 14 was treated over a four year period for acute pharyngitis and acute polyarteritis. She was hospitalized April 29, 1947. In the hospital the temperature varied from 103 to 98.9. Examination showed acute pharyngitis, with acute polyarteritis and an erythematous patchy eruption on trunk and lower extremities; the superficial lymph nodes were enlarged but nontender. The hemoglobin was 11.5 Gm. and red blood cell count 3,990,000 with a white blood cell count varying from 19,300 to 8,500. In the differential count the neutrophils were increased. The clinical diagnoses were acute rheumatic fever, atypical erythema multiforme and possible Hodgkin's disease.

The excised cervical and axillary lymph nodes showed lipomelanotic reticular hyperplasia. The patient was discharged July 12, 1947, after all acute signs and symptoms had subsided.

The patient was last seen on Jan. 16, 1950. No skin lesions had been noted since April 1948; however, a roentgenogram of the hands and wrists showed characteristic changes of rheumatoid arthritis.

CASE 3.—A white man aged 57 was hospitalized Aug. 26, 1949 because of painful swelling of the right ankle which persisted after development of pain in the right calf.

Examination revealed decided epidermophytosis of the feet, enlarged bilateral nontender inguinal lymph nodes and pitting edema of the right ankle.

An excised right inguinal lymph node showed lipomelanotic reticular hyperplasia. The epidermophytosis improved with roentgen ray treatment and local therapy. The swelling of the ankle was considered to be the result of thrombophlebitis secondary to epidermophytosis. On Feb. 24, 1950 the patient had no complaints. The inguinal lymph nodes were still slightly palpable, and epidermophytosis was slight.

CASE 4.—A white woman aged 64 was hospitalized in April 1945 with the complaint of widespread "itchy skin." The illness had begun in 1941, when the skin had become red, rough and scaly.

The examination showed redness, scaling and excoriation of the skin of the trunk and extremities. The right and left axillary and inguinal lymph nodes were enlarged, firm and nontender. The red blood cell count was 3,870,000, with 82 per cent hemoglobin, and the white blood cell count was 10,150. The differential count showed monocytes of the Schilling type. The result in the glucose tolerance test was of the diabetic type.

4. Laipply, T. C.: Lipomelanotic Reticular Hyperplasia of Lymph Nodes, Arch. Int. Med. **81**:19-36 (Jan.) 1948.

Biopsy of the skin revealed abnormal mononuclear cells suggestive of leukemia. Excised inguinal lymph nodes showed reticular cells with sudanotropic material and melanin in the cortex and atypical monocytes in the medulla.

The patient was discharged, slightly improved, with a diagnosis of Schilling's monocytic leukemia and diabetes mellitus. Death occurred two years later from monocytic leukemia.

CASE 5.—A Negro aged 59 was first observed in 1943 because of an eruption on exposed parts of his body. It had occurred during the summer months for several years. The affected skin showed increased pigmentation, scaling and lichenification, accompanied with moderate pruritus. The usual laboratory examinations revealed no abnormality.

Exposure to a mercury vapor lamp produced a strong erythematous reaction after 1½ minutes at 30 inches (75 cm.). The clinical diagnosis was actinic dermatitis. Improvement was so pronounced that the patient was discharged in a few days, but he was readmitted several weeks later.

This time the axillary and inguinal lymph nodes were moderately enlarged, firm and nontender. An excised axillary node revealed the classic picture of the syndrome. A section of the skin showed the epidermis to be distinctly increased in thickness with diffuse hyperkeratinization, patchy parakeratosis and diffuse acanthosis. The dermis was increased in thickness, fibrotic and infiltrated with many lymphocytes, large mononuclear cells and a few eosinophils. The subcutaneous tissue showed similar fibrosis and cellular infiltration. After 18 days' hospitalization the cutaneous lesions disappeared, and the gland returned to normal in three weeks' time. Three weeks later the lymph nodes were no longer enlarged.

CASE 6.—A white woman aged 48 had had an erythematous eruption of the groin and trunk for eight months when first observed, in January 1946. This was accompanied with considerable pruritus. There had been a pronounced loss of weight. The clinical diagnosis of seborrheic dermatitis was made. All the superficial lymph nodes were greatly increased in size, firm and nontender. A psychiatric examination led to the diagnosis of psychoneurosis with marked depression.

Laboratory examinations revealed no abnormality except moderate secondary anemia. A section of the involved skin showed chronic dermatitis. Two inguinal lymph nodes were removed and showed the typical picture of the syndrome; thus, the possibility of lymphoblastoma, which had been strongly considered, was not supported. After 25 days of hospital care and symptomatic treatment the cutaneous lesions and lymph node enlargement were decidedly improved.

CASE 7.—A white man aged 56, a tire maker in a rubber plant, was seen in January 1945 because of a widespread erythematous papular eruption on both anterior tibial surfaces which gradually involved the upper extremities and trunk. The axillary and inguinal lymph nodes were considerably enlarged, being firm, discrete, freely movable and slightly tender.

The basal metabolic rate was + 50. Other examinations revealed no abnormality except a 5 per cent eosinophil count and a white blood cell count of 10,300. A biopsy of the skin of the right forearm showed chronic dermatitis, and a lymph node removed from the left inguinal region showed typical changes of the syndrome. Fifty-three days of hospitalization produced a decided improvement. The basal metabolic rate ranged from + 23 to + 65 with no clinical findings to support a diagnosis of hyperthyroidism.

CASE 8.—A white man aged 46 was hospitalized Jan. 9, 1949 for bilateral inguinal hernia of 15 years' duration. He had worn a truss for 14 years.

The examination showed bilateral reducible indirect inguinal hernia. The skin in the left inguinal region was slightly roughened and pigmented, with pronounced crural lymphadenopathy. The hemoglobin was 16 Gm.; red blood cells, 5,350,000 and white blood cells, 8,000 with the differential count normal.

Bilateral hernioplasty was performed, and a prominent left inguinal lymph node was excised. The lymph node showed reticular hyperplasia, deposition of melanin and scattered eosinophils characteristic of lipomelanotic reticular hyperplasia.

The patient was examined on March 10, 1950, at which time no abnormal physical signs were noted.

CASE 9.—A Negro aged 52 was first observed on Aug. 20, 1946. He had had varicose veins for 10 years, an ulcer of the right leg for eight months and an ulcer of the left leg for two months.

The examination showed an ulcer on the medial aspect of the right leg, 7.6 cm. in diameter; an ulcer of the medial left malleolar area, 1 cm. in diameter; pronounced varicose veins of the lower extremities, and moderately enlarged, slightly tender inguinal lymph nodes of bilateral distribution.

An excised right inguinal lymph node showed slight reticular hyperplasia, scattered eosinophils and melanin and fat in the reticular cells. The patient was last seen Sept. 23, 1946, at which time the ulcers and slight enlargement of the lymph nodes were still present.

CASE 10.—A white woman aged 56 was admitted to the hospital in January 1945 because of an eruption of two years' duration. While working in a tailor shop, she had acquired itching with "breaking out" on the hands, forearms and face. Her own physician had made a diagnosis of monocytic leukemia with cutaneous involvement because of the abnormal peripheral blood smears. The superficial lymph nodes were all enlarged.

The white blood cell count at the time of admission was 12,350 with 54 per cent neutrophils, 3 per cent eosinophils, 10 per cent normal monocytes and 23 per cent abnormal monocytes. The red blood cell count was normal. The urine contained numerous white blood cells. A clinical diagnosis was made of monocytic reticuloendotheliosis or the Schilling type of monocytic leukemia.

A biopsy specimen of the skin of the left forearm was characteristic of lymphoblastoma "consistent with a diagnosis of monocytic leukemia." No eosinophils were present in the dermis. A left inguinal lymph node was removed and showed the microscopic features of lipomelanotic reticular hyperplasia and leukemic infiltration.

Sixteen days of hospitalization produced considerable improvement. Later marked pruritus occurred and, because of arteriosclerotic heart disease and attacks of anxiety hysteria, the patient was transferred to a nursing home. In nine months' time she died, the immediate cause of death being bronchopneumonia. Autopsy revealed widespread monocytic leukosis of the Schilling type. The lymph nodes showed large mononuclear cells with pronounced variation in size and shape, distinct nuclear pleomorphism and acidophilic homogenous cytoplasm.

CASE 11.—A white woman aged 35 was first seen Jan. 9, 1949 because of an itching skin eruption of four weeks' duration. A similar rash noted two years before had lasted three months and spontaneously disappeared. There was a history of chronic alcoholism for several years.

Examination showed an erythematous, papular, patchy, scaly eruption with many excoriations on the face, hands and feet. The liver was 5 fingerbreadths below the costal margin. The cervical, axillary and inguinal lymph nodes were enlarged and nontender; the hemoglobin was 11.5 Gm.; red blood cells were 3,320,000 and white blood cells, 10,000 with the differential count normal. The clinical diagnosis was lymphosarcoma because of the many nodules and severe pruritus.

An inguinal lymph node removed Jan. 26, 1949 was diagnostic of lipomelanotic reticular hyperplasia. On March 20, 1950 the patient was living and well. Cirrhosis was considered the basis for the enlarged liver.

CASE 12.—A Negro aged 46, a sheep herder, was first observed in May 1949 in the Mercy Hospital-Loyola University Clinics. He presented an eruption on the right anterior tibial area which, with intermittent severity, had been present for four years. Recently it had spread to other tibial regions and the upper extremities and trunk. No history of contact etiology was elicited.

Examination showed that there was a symmetrical erythematous eruption on the above-mentioned areas. The inguinal, axillary and epitrochlear lymph nodes were greatly enlarged, especially those of the right crural area. The cutaneous lesions were thought to be associated with the general condition, i. e., a hypertensive cardiovascular-renal disease. Etiology of the latter condition has never been determined.

The blood pressure was 210/130. The leukocyte count was 13,000 with 5 per cent eosinophils. The urine contained numerous granular casts. The blood urea nitrogen was 20.5 mg. per 100 cc., and the blood sugar was 77 mg. per 100 cc. The bone marrow showed increased erythropoiesis. While the patient was in the hospital an axillary lymph node was removed. It showed charac-

teristic anatomic features of lipomelanotic reticular hyperplasia. The changes were more marked in this case than in any of the other cases observed to date. No melanin was ever found in the urine. Skin biopsy revealed no specific features.

After five weeks of hospitalization the widespread dermatitis disappeared either because of local symptomatic therapy or coincident with the decided improvement in the general condition, especially the nephritis.

At the time of writing, June 1, 1950, no cutaneous lesions other than mild residual roughness of the anterior tibial cutaneous areas were present. No lymph nodes were palpable. The patient's general condition was good, but he was still unable to perform any heavy work.

CASE 13.—M. G., a white housewife aged 42, had had an eruption appear on the anterior tibial surfaces in June 1949, while she was under treatment for arthritis. The arthritis was treated with various medications and improved decidedly. The eruption, however, became widespread, and all internal therapy was discontinued; nevertheless, no dermatological improvement was noted.

When observed in late August the patient presented a widespread symmetrical, patchy, erythematous eruption over the lower extremities and trunk. It was intensely pruritic. She had lost considerable weight and strength. The inguinal and axillary lymph nodes were decidedly enlarged, firm, discrete and nontender. The right inguinal lymph nodes were more markedly increased in size, having maximum measurements from 8 to 11 mm. One of these inguinal lymph nodes was excised and showed the picture of lipomelanotic reticular hyperplasia with only a small amount of melanin granules.

Symptomatic therapy gradually resulted in complete disappearance of the cutaneous eruption. At the time of writing lymph nodes were no longer palpable. The patient had regained her former weight and strength. The white blood cell count remained normal at all times. On June 1, 1950 the white blood cell count was 9,300 and the differential count was 69 per cent polymorphonuclear cells, 22 per cent lymphocytes, 6 per cent mononuclear cells, and 3 per cent eosinophils.

CASE 14.—H. B., a white woman aged 48, was first seen in September 1949 with a pruritic eruption in the left crural area consisting of patchy erythematous glistening areas, of several weeks' duration. It had recently spread to the right groin, back, scalp and thorax. It was considered to be seborrheic dermatitis. The crural, axillary and cervical lymph nodes were considerably enlarged, firm and nontender.

The patient's general condition was poor; she had lost a great deal of weight and strength. Results of laboratory examinations were normal except for a hemoglobin count of 74 per cent and red blood cell count of 2,800,000. Examinations of tissue from a cutaneous lesion showed chronic inflammation. An excised inguinal lymph node showed lipomelanotic reticular hyperplasia.

The eruption finally disappeared in four weeks, and the lymph nodes returned to normal in six weeks.

This case illustrates the concomitant occurrence of cutaneous eruption, lymphadenopathy and profound loss of weight and strength. Improvement in the general condition following the disappearance of dermatitis and lymphadenopathy made very unlikely the possibility of lymphoblastoma of any type.

CASE 15.—C. H., a white man aged 52, was first seen about four years ago with a pronounced eruption of the anterior tibial area, of several months' duration. Examination at that time showed a widespread erythematous eruption with marked edema and swelling of the ankles. As this eruption had occurred regularly in the late summer, it was considered of phytogenic origin. Symptomatic therapy produced improvement in a few weeks.

The patient returned in February 1950, with a recurrence, of several weeks' duration, of a patchy, severe, itching erythematous eruption on the trunk and anterior tibial surfaces. The inguinal and axillary lymph nodes were greatly enlarged, firm, and nontender. In a short time the cutaneous lesions became widespread, edematous and exudative. Biopsy of the lesion on the anterior left tibial surface showed subacute dermatitis of a nonspecific type. The excised inguinal node showed all the changes of the syndrome under discussion. Results of all other examinations were normal. At the time of writing, the cutaneous eruption had improved only slightly and the lymph nodes had not decreased in size.

COMMENTS

The cases recorded in this paper are illustrative of a distinct clinicopathologic entity which, although not generally recognized, is probably not uncommon. The clinical manifestations include dermatitis, usually with severe pruritus and marked enlargement of lymph nodes. The cutaneous lesions vary in degree and distribution. There are usually considerable erythema, scaling and excoriations. A typical exfoliative dermatitis may develop. The lymphadenopathy may be widespread but is in most instances particularly pronounced in the axillary and inguinal regions. The enlarged lymph nodes are characteristically firm, discrete and nontender. Other manifestations of lymphoblastoma, such as persistent elevation of the white blood cell count, abnormal white cells in the circulating blood, anemia and splenomegaly, are absent in the uncomplicated cases.

Biopsies of skin usually reveal chronic dermatitis without a characteristic microscopic picture. The epidermis may be slightly thickened. The cellular infiltration of the dermis is made up of lymphocytes, large mononuclear cells and eosinophils. In some instances an occasional mononuclear cell contains melanin, but in none is there noteworthy cellular pleomorphism.

The lymph nodes are enlarged and slightly softer than usual and have intact capsules. They section with reduced resistance and have bulging pale yellow cut surfaces. The yellow color is suggestive of the presence of fat, but rarely is brown mottling due to the melanin pigmentation observed. The microscopic picture of the lymph nodes is characteristic. The normal architectural pattern may be slightly altered, but it is never completely obscured. The predominant cell is the large mononuclear (reticular) cell with abundant faintly acidophilic cytoplasm that is frequently vacuolated. The cytoplasmic vacuolization is due to sudanotropic material, which is readily demonstrated with sudan IV stain. These large cells are particularly conspicuous in the cortices, where when abundant they alter the architectural pattern. The lymph follicles may be slightly enlarged with distinct secondary centers, but they usually appear to be decreased in number because of wide separation by the large reticular cells in the cortical region. A varying number of large mononuclear cells contain granular dark brown pigment, which is identified as melanin by the lack of a reaction to potassium ferrocyanide and hydrochloric acid, black coloration with silver nitrate and solubility in hydrogen peroxide. Eosinophils, although not numerous, are always present. Plasma cells may be noted, but they are usually few. Fibrosis and giant cells are not part of the microscopic picture. Cellular pleomorphism is usually not striking. (In this respect the case reported by Soloff, in which there was appreciable cellular pleomorphism in the lymph node, was atypical.)

The dermatitis is considered to be primary and the changes in the lymph nodes secondary. The inflammation of the skin causes hyperplasia of the draining lymph nodes. The scratching induced by pruritus probably brings about increased formation and liberation of melanin from cells of the epidermis. Such pigment would then be transported to regional lymph nodes and phagocytosed by reticular cells. Thus the amount of melanin pigmentation of the lymph nodes is dependent on the duration and severity of the pruritic dermatitis. The sudanotropic material in the reticular cells is probably secondary to excessive amounts of fat entering the cutaneous lymphatic vessels as a result of scratching and injury.

In normal lymph nodes or in those which are the seat of ordinary follicular or reticular hyperplasia, melanin and fat are usually absent; however, they may be present in otherwise normal lymph nodes, as was demonstrated by Keye.[5] For comparison with the lymph nodes in the cases reported in this paper, 40 lymph nodes which were the seat of reticular and follicular hyperplasia were examined and stained with sudan IV. In some there were a few reticular cells that contained sudanotropic droplets, but in none was the amount of sudanotropic material as great as in the lymph nodes which were the seat of lipomelanotic reticular hyperplasia.

The mechanism of development of lipomelanotic reticular hyperplasia of lymph nodes is such that it can theoretically occur in any condition of inflammation and itching of the skin. Thus, the presence in lymph nodes of changes characteristic of lipomelanotic reticular hyperplasia does not of necessity preclude the concomitant existence of a lymphoblastoma. Thus, in cases 4 and 10 the changes in the blood, skin and lymph nodes were consistent with a diagnosis of monocytic leukosis of Schilling type. It should be noted that in both instances the changes in superficial lymph nodes were those of lipomelanotic reticular hyperplasia as well as of monocytic leukemia. (At the time of autopsy the microscopic changes in the thymus, liver, spleen, lymph nodes, kidney and bone marrow in case 4 were different from those in lipomelanotic reticular hyperplasia. In these organs the large mononuclear cells showed considerable variations in size and shape, distinct nuclear pleomorphism and moderately acidophilic, homogeneous, nonvacuolated cytoplasm without sudanotropic droplets. None of the lymph nodes contained melanin or eosinophils. From an anatomic standpoint, therefore, the microscopic features of Schilling's monocytic leukosis and those of lipomelanotic reticular hyperplasia of lymph nodes are easily distinguished. Nevertheless, patients with the Schilling type of monocytic leukosis [6] usually have a relatively long course of illness, and cutaneous lesions with pruritus may develop.) It is essential, therefore, that the possibility of the existence of this type of monocytic leukemia be kept in mind in the treatment of patients who have the clinicopathologic entity of pruritic dermatitis and lipomelanotic reticular hyperplasia of lymph nodes. Bluefarb and Webster [7] have just reported two cases of lipomelanotic reticulosis which developed into mycosis fungoides, indicating that some cases may possibly eventuate in lymphoblastoma. A review of this type of case, they believe, brings to light the suggestion of a toxic or irritative agent which stimulates the entire reticuloendothelial group of cells to hyperplasia and some of the cells even to neoplasia. However, the lymph node changes in this type may well be only incidental to the malignant changes. Obermayer and Fox [8] have

5. Keye, K. R.: Über die natürliche Abwanderung des Pigments aus den Haut in die Lymphdrüsen bei Pferden, Zentralbl. allg. Path. u. path. Anat. **34**:57-60, 1923.

6. Montgomery, H., and Watkins, C. H.: Monocytic Leukemia: Cutaneous Manifestations of the Naegeli and Schilling Types; Hemocytologic Differentiation, Arch. Int. Med. **60**:51-63 (July) 1937.

7. Bluefarb, S. M., and Webster, J. R.: Lipomelanotic Reticulosis, Arch. Dermat. & Syph. **61**:830-841 (May) 1950.

8. Obermayer, M. E., and Fox, E. T.: Lipomelanotic Reticulosis of Lymph Nodes in a Case of Lichen Planus, Arch. Dermat. & Syph. **60**:609-613 (Oct.) 1949.

recently reported this characteristic lymph node involvement in a case of lichen planus. They cited Jadassohn [9] as having described some peculiar histological lymph node changes in a case of pityriasis rubra (Hebra). Five other case reports [10] have been made under various confusing terminologies. The term here used is lengthy but is believed to be very descriptive. In the fifth edition of Gould's dictionary [11] the term reticulosis is defined as meaning reticulocytosis, or an excess over the normal percentage of reticulocytes in peripheral blood, simulating leukemia. It seems that it would be better for all to use one descriptive term which is as accurate as possible.

SUMMARY

Chronic dermatitis, particularly when accompanied with pruritus, may result in a characteristic type of hyperplasia of lymph nodes. The lymph nodes are usually moderately enlarged, discrete, firm and nontender. On gross examination they frequently have a yellow tinge and occasionally show dark brown mottling. The microscopic features include slight distortion of the normal architectural pattern, severe hyperplasia of reticular cells, which contain melanin and sudanotropic droplets, and infiltration with eosinophils. The secondary centers of the lymph follicles are sometimes evident, but the notable proliferation of reticular cells is in the pulp of the lymph nodes.

Fifteen cases of various types of dermatitis and this type of hyperplasia of lymph nodes are reported and their status at the time of writing described. Because of the prominence of the lymphadenopathy an incorrect clinical diagnosis of lymphoblastoma may be made in many instances. A diagnosis of lipomelanotic reticular hyperplasia of lymph nodes does not preclude the possibility of the concomitant existence of a lymphoblastoma. Thus, in two of the cases there were changes in the blood and tissues that warranted the diagnosis of Schilling's monocytic leukosis. Lipomelanotic reticular hyperplasia of lymph nodes is a benign lesion that is secondary to chronic pruritic dermatitis. Although it may be associated with leukemia, Hodgkin's disease or lymphosarcoma it has no direct relationship to them. This entity is believed to be much commoner than indicated by the number of cases recorded in the literature.

Suite 309, 700 North Michigan Avenue (11).

9. Jadassohn, J.: Über die pityriasis rubra (Hebra) und ihre Beziehungen zur Tuberculose (nebst Bemerkungen über Pigmentverschleppung aus der Haut), Arch. Dermat. u. Syph. **23**:941-974, 1891, cited by Obermayer and Fox.[8]

10. Ramel, E.: Neuropathic Eczema, Brit. J. Dermat. **36**:247, 1947. Sulzberger, M. B., and Garbe, W.: Nine Cases of Distinctive Discoid and Lichenoid Dermatosis, Arch. Dermat. & Syph. **36**:247 (Aug.) 1937. Pinetti, P.: Contributo alla conoscenza delle adenopatie secondarie a dermatosi croniche e dei loro rapporti con la migrazione linfatica del pigmento cutaneo, Boll. Soc. med.-chir., Pavia **52**:295, 1938. Cannon, A. B.: Allergic Dermatitis Simulating Lymphoblastoma, Arch. Dermat. & Syph. **39**:846 (May) 1939. Oliver, E. A., and Greenberg, A.: Generalized Erythroderma with Lipomelanotic Reticulosis (Pautrier and Woringer), Arch. Dermat. & Syph. **54**:621 (Nov.) 1946.

11. Gould, J. M.: Medical Dictionary, ed. 5, revised by C. V. Brownlow, Philadelphia, The Blakiston Company, 1941.

ABSTRACT OF DISCUSSION

COLONEL FRANKLIN H. GRAUER, Washington, D. C.: This interesting presentation has called attention to a distinct clinicopathologic entity which, although not generally recognized, is probably not uncommon.

As a basis for the following discussion, an analysis was made of a sample of 32 cases of lipomelanotic reticular hyperplasia of lymph nodes, selected at random from the files of the Armed Forces Institute of Pathology.

A study of these cases reveals that any extensive, chronic or chronic-recurrent pruritic dermatitis, particularly of an exfoliative type, may be associated with a generalized superficial lymphadenitis. This lymphadenitis is characterized by a proliferation of reticulum cells, by phagocytosis of melanin, hemosiderin and, occasionally, fat and by pleomorphic cellular infiltrations consisting of eosinophils, neutrophils and plasma cells. The basic architecture of the lymph node is preserved.

Lipomelanotic reticular hyperplasia of lymph nodes may be associated not only with the various dermatoses presented by Drs. Laipply and White but also with some types of lymphoblastoma, atopic dermatitis, dermatitis herpetiformis, pityriasis rubra (Hebra), parapsoriasis, eczematoid dermatitis, dermatitis medicamentosa due to arsenic and possibly at times to mercury, bismuth or bromides, chronic lichenified eczema, prurigo, exudative chronic discoid and lichenoid dermatosis (Sulzberger and Garbe), allergic dermatitis simulating lymphoblastoma as described by Cannon and chronic dermatitis of nonspecific type. In our series it was associated with psoriasis with superimposed exfoliative dermatitis not infrequently, and it has been reported with lichen planus and generalized eruptions originating as contact dermatitis of the hands.

A study of our cases reveals that the most frequent cause for submitting cutaneous and lymph node biopsies was that the clinician either suspected or wanted to rule out Hodgkin's disease, lymphosarcoma with cutaneous involvement or mycosis fungoides with secondary lymph node infiltrations. Helwig of the Armed Forces Institute of Pathology agrees with Drs. Laipply and White that lipomelanotic reticular hyperplasia of lymph nodes is secondary to the inflammatory reaction in the skin and has no direct relationship to mycosis fungoides or other lymphoblastomas, although both disorders may at times be encountered in the same lymph node. He does not believe that it bears any relation to giant follicular hyperplasia of lymph nodes and spleen, i. e., Brill-Symmers disease.

Hurwitt feels that the histological changes in lipomelanotic reticular hyperplasia of lymph nodes differ from those observed in mycosis fungoides, Hodgkin's disease and follicular lymphoma, which they superficially resemble, by absence of destruction of the basic architecture of the lymph node, the absence of the Sternberg-Reed cells and the presence of phagocytic activity in the reticulum cells. He believes that the claim for its essentially benign character has been substantiated by prolonged follow-up observation and that this hyperplasia of lymph nodes may undergo spontaneous involution. There is another school of thought, however, which believes that lipomelanotic reticular hyperplasia of lymph nodes may occasionally develop into a malignant process. Only a prolonged follow-up of a large series of cases will eventually clarify this issue, but, if I may judge on the basis of the information at hand, if malignant change does superimpose itself on this disorder its doing so must be extremely rare. It is interesting to note that the majority of the patients have blood eosinophilia and that on occasions iron pigment in addition to melanin may be encountered in the lymph nodes. This last observation was noted in two of our cases.

In conclusion, I should like to add that, although we do not wish to attach undue significance to terminology, we are inclined to agree with Hurwitt that the name of "lipomelanotic reticulosis" or "reticular hyperplasia of lymph nodes" is not sufficiently comprehensive since it fails to emphasize both the outstanding features of the disorder and the fact that the lymphadenitis is secondary and dependent on the skin disease. We prefer the name originally applied by him to this condition, i. e., dermatopathic lymphadenitis.

I wish to congratulate Drs. Laipply and White on their interesting paper and scientific exhibit dealing with this important subject.

DR. ERNEST T. FOX, Oceanside, Calif: Dr. Grauer has emphasized sufficiently the fact that this condition is a benign type of abnormality. With regard to the causative factors of this peculiar enlargement of the lymph nodes, Dr. Overmayer and I feel that it is not the dermatitis which is the etiologic agent, but rather trauma secondary to the pruritis which that dermatitis has caused. In other words, repeated and long-continued scratching and irritation of the skin seem to be the essential factor.

The reason for this abnormality, however, has not yet been determined. Why should a great variety of pruritic dermatoses cause the occurrence of this abnormality of the lymph nodes in only a few instances? One might postulate that there may be some microbic factor, such as a virus, which has not hitherto been discovered; certainly this possibility must be investigated.

I agree with Dr. White that the term "lipomelanotic reticulosis" is not as good a term as "lipomelanotic reticular hyperplasia of the lymph nodes." Dr. White did not mention in his discussion here today several of the cases which were displayed in the scientific exhibit. One instance of lipomelanotic reticular hyperplasia was apparently produced by chronic ulceration of the leg; there was no mention of pruritus in this case. Another was caused apparently by the presence in one person of long-continued bilateral hernia. Since the presence of pruritus was not mentioned in the history of either of these cases, it is again difficult to see what was the causative agent in bringing about the unusual abnormality of the inguinal nodes.

DR. HAROLD C. FISHMAN, Beverly Hills, Calif.: I felt very privileged today to hear the excellent presentation of Dr. White. My attention was first directed to this entity when a post-mortem examination was done on a patient at the County Hospital in Los Angeles in 1939. A clinical diagnosis of a melanotic carcinoma of the bowel, with marked pigmentation of the skin, had been made by the medical staff. However, the man died of another cause, and then the new clinical entity was called to the attention of the medical and dermatological staffs.

Since that time, except for the interruption of the war years, we have collected other cases, accounts of which are to be published.

I personally am heartily in agreement with the points that were brought out by Dr. White. Other men from different parts of the country with whom I have talked feel the same way. I think the entity is pretty well recognized now, and by independent groups, which fact was rather interesting to me.

In my experience usually there was quite marked pigmentation of the skin, which observation was not especially emphasized here. Perhaps the melanin deposited deep in the cutis by the melanophores may be a possible factor in the enlargement of the lymph nodes.

In one case in a Negro there was pronounced depigmentation.

DR. LOUIS H. WINER, Los Angeles: I am of the opinion that this condition is not an entity but a group of characteristic observations based primarily on the colliquative or liquefaction degeneration of the basal cells which contain melanotic pigment. Thus, the melanin is precipitated into the cutis, where it is picked up by the lymphatics and carried to the regional lymph nodes. Here it causes an obstruction or a nonspecific inflammatory reaction much as occurs in the fatty transformation in necrobiosis lipoidica diabeticorum of the skin. I would consider this condition a type of necrobiosis of lymph nodes secondary to melanin deposition in the lymph nodes.

DR. LAWRENCE C. GOLDBERG, Cincinnati: After listening to this paper and looking backward I think I now have an explanation for the increased pigmentation found in the glands of patients with exudative cases of quinacrine dermatosis.

DR. HYMAN I. GOLDSTEIN, Camden, N. J.: I simply rise to appeal to this Section, and to all dermatologists, to go a little easy on us poor, long-suffering clinicians with the extensive nomenclature that dermatology has already developed. When I attempt to look up some of the newer nomenclature that is developing rapidly in the field of dermatology, it is with considerable fear and trepidation!

I think that this condition which has been presented this morning is definitely neither a "syndrome" nor an "entity," any more than stellar nevi or telangiectasis and varices, with itching and cirrhosis of the liver, would be. A syndrome is a complete complex of symptoms—the sum of signs and symptoms occurring together of any definite morbid state.

DR. CLEVELAND J. WHITE, Chicago: Sometimes a paper is valuable on account of the discussion, and I certainly thank the discussers for their fine comments. I fully agree with them all the way along the line that the condition is a symptom complex—what we are going to call it remains to be seen. The name we put down at least describes the observations, even if it does look like a brief textbook description.

Dr. Grauer's discussion was certainly a very valuable addition to the whole situation, especially his addition of reports of many more cases well studied. I think the term "dermatitis lymphadenitis" is very apropos clinically and may well be the term best suited for this syndrome.

With regard to Dr. Fox's remarks, we had two cases that were in the group he described; the absence of pruritus makes one worry for the moment to make sure there is not possibly a lymphoblastoma. Two of the cases were not recorded on the charts; we had to cut down to make the size of the charts fit the exhibit space. One other patient had ulcerations—still has them—and had a dermatitis of the type that was traumatic.

Dr. Fishman's case was extremely interesting and brings up the melanin problem. In such cases of melanomaderma all patients were tested for melanin and the urine examinations were negative.

I believe Dr. Winer's thinking is like that of the rest of us. The etiology may well be on the basis that he outlines. We have no specific data on that point at the present time.

Dr. Goldstein's further comments bring out that the disorder is a symptom complex and that we should try to recognize all possible angles.

Dr. Laipply and I feel that the symptom complex per se is essentially a benign condition.

MYCOLOGIC AND HISTOLOGIC TECHNICS IN THE STUDY OF SUPERFICIAL FUNGOUS INFECTIONS

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THE FEATURES of certain superficial fungous infections may be so typical that the clinical diagnosis is almost certain to be correct. This is certainly true for most cases of tinea (pityriasis) versicolor, particularly if the patient is observed during the summer months when the patches are deeply pigmented. Tinea infection may also be strongly suspected in many instances of circinate lesions of the skin in scalp disease in children, in chronic paronychia and in an intertriginous rash of the feet, particularly if the nails also are involved.

With increasing experience the clinician may develop the ability not only to suspect a mycotic disorder but also to be reasonably certain of the causative fungus. The syndrome of infection due to Trichophyton purpureum has been described,[1] and the description is commonly accepted. The work of Hopkins and associates[2] during the last war indicates that in a young adult group and with recent infection the clinical signs may deviate from the usual picture and acute manifestations be present, with findings rarely observed in civilian practice and under normal peacetime conditions. That there are many clinical signs and symptoms the knowledge of which the good observer may use to advantage is illustrated by the report of Alkiewicz,[3] who drew attention to a sign of onychomycosis consisting of a delicate white net arranged parallel with the transverse axis of the nail, visible through a magnifying glass only after application of a drop of cedar oil. This is a network of air spaces due to destruction of nail substance by the mycelium. It is an almost certain sign of fungous disease.

The foregoing comments indicate that it is possible for an experienced clinician to diagnose and treat many fungous diseases without benefit of laboratory confir-

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Read before the Section on Dermatology and Syphilology at the Ninety-Ninth Annual Session of the American Medical Association, San Francisco, June 29, 1950.

1. Lewis, G. M.; Montgomery, R. M., and Hopper, M. E.: Cutaneous Manifestations of Trichophyton Purpureum (Bang), Arch. Dermat. & Syph. **37**:823 (May) 1938.

2. Hopkins, J. G.; Hillegas, A. B.; Ledin, R. B.; Rebell, G. C., and Camp, E.: Dermatophytosis at an Infantry Post: Incidence and Characteristics of Infections by 3 Species of Fungi, J. Invest. Dermat. **8**:291 (June) 1947.

3. Alkiewicz, J.: Transverse Net in Diagnosis of Onychomycosis, Arch. Dermat. & Syph. **58**:385 (Oct.) 1948.

mation and be able to cure a fairly high percentage of the patients. One might question, then, the necessity for the routine use of laboratory diagnostic procedures in what appear to be typical instances of superficial fungous disease. On reflection it is apparent that with mycotic disease, as with any other type of infection, laboratory confirmation of the clinical impression may be essential in only a minority of patients. However, screening out patients as lacking the need for laboratory verification may be impossible. Furthermore, as it is well known that fungous

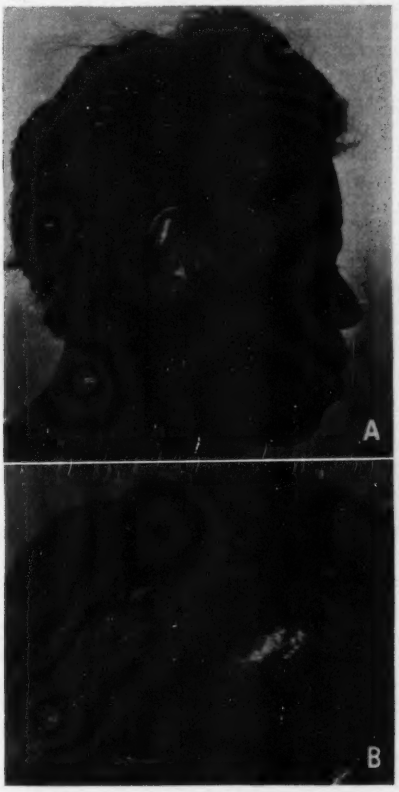


Fig. 1.—The value of routine cultures of all scalp lesions irrespective of the clinical appearance is exemplified by the finding of T. purpureum in *A* and T. crateriforme in *B*. In both instances the fluorescence test had negative results and the direct mount did not reveal fungi.

disease may simulate many other skin, nail and hair disorders, the simplest or most typical eruption may yield an unusual fungus; without the laboratory one might be unaware that the causal micro-organism had far-reaching significance not only to the patient but also in the study of epidemiologic patterns. The actual demonstration of a pathogenic organism in culture is irrefutable proof and is always useful information prior to the beginning of therapy. It may be even more valuable later, when the disease has been treated with partial success or when a treatment reaction has

complicated the picture. Our present understanding of fungous diseases is based primarily on what has been determined from the correlation of clinical and laboratory data. For several years the symptom complex of dermatophytosis was used incorrectly as an explanation for eczematous lesions of the hand. Failure to demonstrate fungi in repeated scrapings from hundreds of these patients was a necessary procedure in order to focus attention on this error.

In obscure diseases of the skin, particularly if the intertriginous areas are involved or if the lesions are vesicular or scaly or the outline of the involved skin tends to be sharply delineated, the routine use of the mycology laboratory will be most helpful. Our practice of hunting for fungi not only when the clinical diagnosis is strongly suggestive but also when the differential diagnosis includes fungous disease is often rewarding but is no doubt partially responsible for our failure to report laboratory confirmation in approximately 60 per cent of patients. There still remains a small but puzzling group with conditions clinically suggestive of fungous disease but in which the laboratory findings are either partially or totally negative. At this time we are unable to offer an adequate explanation but in

Fig. 2.—Without a high index of suspicion, a nondescript lesion such as this would not have been cultured. Microsporum fulvum was isolated.

common with other workers believe that our technical methods might be improved sufficiently to reduce further the number in this small but important group.

Careful scrutiny of the literature pertaining to technical advances during recent years reveals a paucity of original methods that are immediately useful. Most of the articles are in the nature of confirmation of existing knowledge or give an original presentation which is either impractical or less definitive or useful than existing measures. There is also the unfortunate and happily small group of papers in which factual data has been misinterpreted and erroneous conclusions drawn.

OBTAINING MATERIAL FOR MYCOLOGIC EXAMINATION

Collection of material is for two purposes: first, to demonstrate fungi in a direct mount and, second, to culture out the offending micro-organism. If one is to obtain good results consistently, it is necessary to develop methods that will eliminate contaminating bacteria and fungi as well as give the best opportunity for positive results. In general, one selects lesions of recent origin and if possible untreated. Material from the periphery of a lesion is most likely to contain the fungous elements. It is our practice to sponge over the area from which the speci-

men is to be taken with either 70 per cent ethyl alcohol or a 0.1 per cent solution of benzalkonium (zephiran®) chloride. The specimen may be collected on the blade of a scalpel, preferably one that is somewhat dull from use. The first scrapings are discarded; specimens for examination then are placed on a clean glass slide ready for preparation with potassium hydroxide solution, and then the second specimen is implanted directly onto the culture medium by slashing the blade across the surface of the medium. In this way specimens are collected from glabrous skin, hairy skin, nail tissue and the surface of the tongue or other mucous membranes. If the operation is gently performed, material may be collected by this method even from paronychial tissue, although in this situation we often use a sterile applicator rather than a scalpel. In order to obtain the best results it is desirable to transfer the material directly to the surface of a culture medium rather than to send it in envelopes or in other ways to a laboratory.

THE FLUORESCENCE TEST

The filtered ultraviolet rays are valuable chiefly in the diagnosis of tinea capitis and in determining when cure has taken place. They are occasionally used to demonstrate fluorescence in lanugo hairs in tinea circinata, in the affected hairs in tinea barbae due to a Trichophyton of the endothrix type and in the skin of patches of tinea versicolor. The black light cannot be depended on to show fluorescence in scalp infections due to Trichophyton crateriforme. These findings have been reported by many workers and are now common knowledge. We have learned to interpret with caution the negative findings in instances when tinea capitis is probable. In a recent patient with tinea capitis the results of the fluorescence test became negative after several months of treatment with a copper compound. In spite of the negative observations on the fluorescence test, positive cultures were repeatedly obtained. The use of the rays in distinguishing certain fungous colonies has also come into fairly wide use.[4] If one wishes to obtain uniform and satisfactory results in the diagnosis and study of the above-mentioned diseases and in the differentiation of fungous cultures it is necessary to select for use one of the better grade commercial lamps constructed for this purpose. The available black light will be satisfactory if the source of the ultraviolet rays is strong and the filter used is of the order of Corning glass violet ultra no. 586. A unit such as the Westinghouse purple X bulb is interesting but should not be considered dependable for medical use as it is not to be trusted to screen out noninfected children[5] and is useless in the differentiation of fungous cultures. The expenditure of $50 to $100 is necessary if one is to be equipped with an adequate lamp.

THE DIRECT MOUNT

An immediate examination of material collected from a patient may reveal the presence of fungous elements and allows a definite or provisional diagnosis of

4. Lewis, G. M.: Fluorescence of Fungus Colonies with Filtered Ultraviolet Radiation (Wood's Filter): An Aid in Determination of Species; Preliminary Report, Arch. Dermat. & Syph. **31**:329 (March) 1935.

5. Dennie, C. C., and Morgan, D. B.: Use of Purple X Bulb in Diagnosis of Fungous Disease of Scalp, Arch. Dermat. & Syph. **55**:396 (March) 1947. O'Farrell, N. M.: Differentiation of Microsporon Audouini from Microsporon Lanosum by Fluorescence, Arch. Dermat. & Syph. **57**:919 (May) 1948.

mycotic disease. The usual and for the most part satisfactory procedure is to add a drop or two of 10 to 15 per cent potassium hydroxide solution to the material and place a cover slip over this preparation. If the material is not too thick, the alkali digests it fairly rapidly and the preparation may be examined under the microscope within a few minutes. For thicker sections or nail tissue it may be advisable to warm the preparation gently, but care should be taken that the specimen does not boil. Green and Shepard [6] have drawn attention to a possible source of error in the resemblance of hyphae to elastic fibers. It should also be kept in mind that it is seldom possible to be certain that circinate bodies resembling spores are not extraneous material such as oil droplets. It is a safe rule to limit the designation "positive" to slides in which segmented hyphae can be demonstrated; exceptions, of course, are slides with hairs in which the mosaic pattern is present.

CULTURE MEDIUMS AND METHODS

According to individual preference, there may be considerable variation in the composition of culture mediums that may be used to isolate fungi. The advice which we have given to many students is to select a medium known to be efficient and for which the ingredients will probably always be available. Minor variations in the composition of the medium may result in tremendous changes in the gross appearance of the fungi, perhaps the commonest reason for confusion experienced by the novice. The composition of our isolation medium is as follows:

Dextrose (technical)	4 per cent
Peptone (Difco)	1 per cent
Agar (powdered)	2 per cent
Water (tap), sufficient to make	100 per cent

(The pH varies from 5.8 to 6.2.)

It is useful also to have available corn meal agar, particularly for the isolation of Candida (Monilia) albicans, as well as several other mediums for special work.[7] In order that certain characteristics of fungi may be developed it is sometimes necessary to add various minerals, proteins, vitamins and the like. It has been our experience that none of these enriched mediums or mediums containing dyes and inhibitors have assisted in the primary isolation of fungi.

It has also been our experience that little or nothing is gained by the use of microculture technics for primary isolation.[8] Such procedures are time-consuming and technically difficult. The incidence of contamination is high and may sometimes escape detection. A noteworthy contribution to the simplification of the technical phases of culturing fungi has recently been made by Wilson and Plunkett.[9]

6. Green, W. S., and Shepard, M. C.: Semblance of Elastic Tissue to Mycelium in Potassium Hydroxide Preparations, Arch. Dermat. & Syph. **52**:115 (Aug.) 1945.

7. Lewis, G. M., and Hopper, M. S.: An Introduction to Medical Mycology, ed. 3, Chicago, The Year Book Publishers, Inc., 1948.

8. Zimerinov, A. A., and Rafalovich, S. M.: Attempt to Investigate Fungus Cultures in Hanging Drop: Preliminary Report, Brit. J. Dermat. **60**:238 (July-Aug.) 1948.

9. Wilson, J. W., and Plunkett, O. A.: Practical Medical Mycology: The Culture of Fungi as an Office Procedure, Arch. Dermat. & Syph. **59**:414 (April) 1949; Practical Medical Mycology: A Discussion of Simplified Laboratory Methods, The Practitioner **163**:523 (Dec.) 1949.

Dissatisfied with the usual test tube method, they have selected from over 300 varieties of small glass bottles a small, flat, perfume type flask with a plastic top. In addition to its convenience, this bottle has the advantage that it may be used only once and discarded with less cost than that required to clean and wash test tubes. It is hoped that the simplicity of the Wilson and Plunkett technic will provide needed help and stimulation so that practitioners will make culturing a routine procedure.

STAINS

We have not found any staining technic to be advisable for routine use in isolating fungi from superficial mycotic infections. Stains are useful when one wishes to preserve permanently a specimen and to preserve culture mounts. For this purpose methylene blue counterstained with a weak alcoholic solution of eosin has been found adequate.

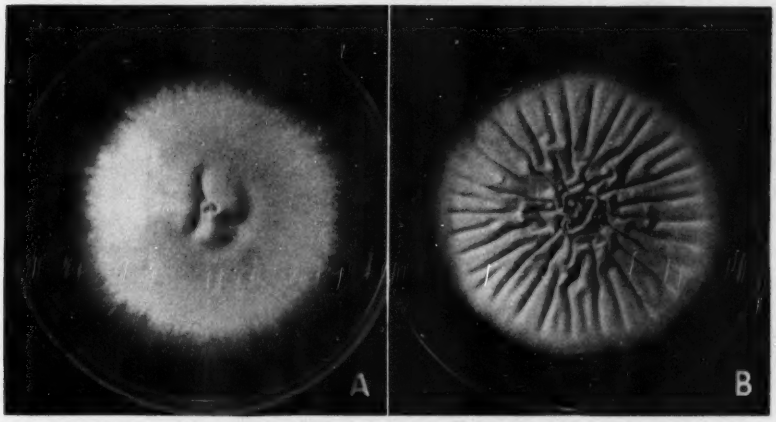


Fig. 3.—Variation in cultural characteristics of T. crateriforme depending on the composition of the medium. *A*, appearance on dextrose isolation medium. *B*, development of radial grooves and lighter pigmentation when fungus was grown on a medium using 6 per cent sorghum instead of dextrose.

PATHOLOGIC FINDINGS

While our investigation is incomplete, preliminary studies indicate that little help in the diagnosis of superficial fungous disease may be expected from the study of histologic sections. The material was prepared and stained with hematoxylin and eosin by the Gram technic, with pyronin and methyl green and by the Hastings method. Fungous elements were occasionally observed but not in every instance, even when the whole block was sectioned. All the superficial fungous diseases reveal changes of a superficial exudative process. It was impossible to distinguish differences in the histologic picture according to species of infecting micro-organism. Sagher [10] reported an interesting study of fungus-infected nails. He noted that the

10. Sagher, F.: Histologic Examinations of Fungous Infections of Nails, J. Invest. Dermat. **11**:337 (Nov.) 1948.

fungi were more superficial in infections caused by Trichophyton violaceum in comparison with those due to Trichophyton purpureum. He also thought it possible to rule out as saprophytes some of the fungi residing superficially but considered other species of the common saprophytes to be invasive in some instances.

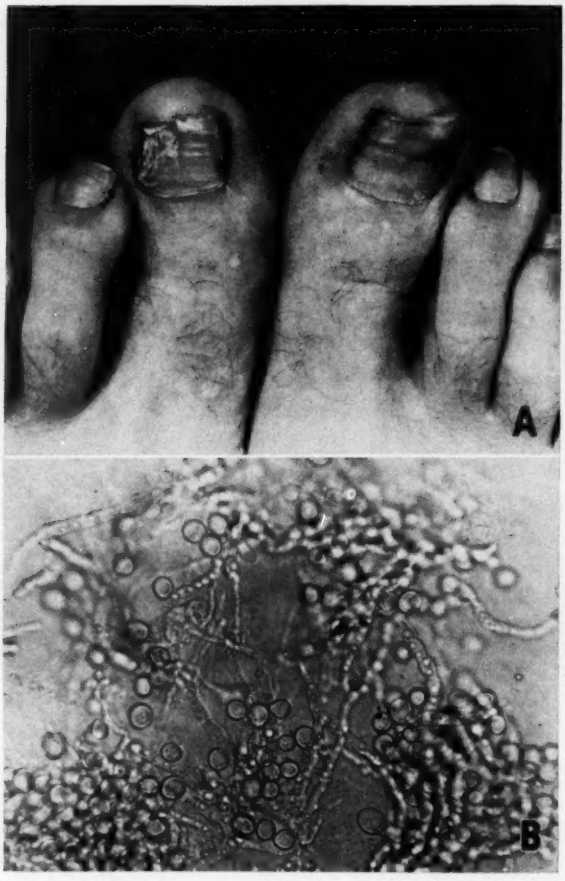


Fig. 4.—*A*, onychomycosis due to Scopulariopsis brevicaulis. Care should be exercised to determine whether fungi that are usually saprophytic are not incidental and masking the real pathogen, which is often deeper. *B*, filaments and spores in a direct mount. Finding the large round spores is suggestive of the micro-organism.

INTERPRETATION OF LABORATORY DATA

In the direct mount it is seldom possible to identify a fungus as pathogenic. Notable exceptions are the findings in scrapings of tinea versicolor, occasionally in moniliasis (particularly thrush) and in hairs invaded by Achorion schoenleini. It is also occasionally possible to identify a saprophytic organism. With cultures

it is considered sound practice to attach significance to the finding of a known pathogen, particularly if the clinical findings are in agreement. For example, if one obtains a specimen of nail tissue, taking the appropriate precautions already mentioned, and the clinical features include yellowish discoloration, friability and opacity of the nail plate, one would not be surprised to culture out T. purpureum and would be justified in classifying this as the cause. However, if a species of Penicillium or Aspergillus were isolated, great care should be exercised in attaching pathogenicity to this isolate. A report by Bereston and Waring [11] of Aspergillus infection of nails leaves room for considerable doubt that the basic cause of the infection was discovered. These authors reported 13 cases, six of which were followed for complete studies. Two of the six were double infections with T. purpureum, and from our experience [12] we feel it is probable that the latter microorganism was the real invader in the other four as well. The temptation to report new and exotic causes for disease should not allow one to lose a sense of perspective and to disregard the necessity for a healthy skepticism. Many of the common fungi will occasionally lose some of their cultural characteristics. For instance, Microsporum lanosum may fail to develop typical yellow pigment in the substrate. In such a situation the novice may be hard pressed to make a correct interpretation if he depends on the pigmentation alone for identification.

With the fluorescence test some experience is necessary in order to rule out extraneous material which is also fluorescent. However, if the bright green fluorescent appearance of infected fungous hairs is repeatedly observed, one will develop assurance that this appearance is characteristic. Absence of fluorescence when expected may be due to (*a*) poor equipment, (*b*) loss of hair due to spontaneous or therapeutic cure, (*c*) masking of the disease by an associated dermatitis or stain from treatment and/or (*d*) the infection's being of an ectothrix or an endothrix Trichophyton variety, in which the fluorescence is less bright. Of course the absence of anticipated fluorescence could also be due to a mistaken diagnosis.

The trichophytin test is often helpful.[13] While a positive reaction to the trichophytin test may not be diagnostic for an eruption present at the time of the test it does mean infection with a dermatophyte. Thus, if the patient is a child or a young adult without previous history of an acute inflammatory disease the positive reaction may be significant. A negative reaction to trichophytin may help to exclude the diagnosis of fungous infection when the presenting disorder is of inflammatory type.

SUMMARY

The methods described in this paper for the most part have been in common use for many years. Material for direct mount or for culturing should be collected with care. There is a reasonable choice in the composition of the medium for isolation, but it is important to become familiar with the appearances of a colony

11. Bereston, W. S., and Waring, W. S.: Aspergillus Infection of Nails, Arch. Dermat. & Syph. **54**:552 (Nov.) 1946.

12. Lewis, G. M., and Hopper, M. E.: Concurrent, Combined and Consecutive Fungous Infections of Skin, Arch. Dermat. & Syph. **47**:27 (Jan.) 1943.

13. Lewis, G. M.; MacKee, G. M., and Hopper, M. S.: The Trichophytin Test: Its Value as a Diagnostic Aid, Arch. Dermat. & Syph. **38**:713 (Nov.) 1938.

for a particular medium. Attributing pathogenicity to an organism isolated from diseased tissue will often be difficult, particularly when the fungus is a so-called contaminant. Many of the stains which have been developed during the past few years are useful in the study of fungi but have no special merit in regard to their primary isolation. In histologic sections of material removed from a biopsy or proved fungous infections, fungi are sometimes demonstrated. The histologic picture is not definitive, and no pathologic characteristics have been noted thereby which would allow one to suggest in any particular case that a certain microorganism was responsible for the disease.

ABSTRACT OF DISCUSSION

Dr. Sture A. M. Johnson, Madison, Wis.: Dr. Lewis and his group are to be congratulated for their practical paper covering the laboratory procedures to follow in isolating and identifying fungi.

The clinical appearance of certain dermatological conditions due to fungi may be so characteristic that the experienced clinician will not only make the proper dermatological diagnosis but will also know the causative organism before laboratory confirmation. However, some of the pitfalls of this procedure become evident, when for instance, one uses the presence or lack of inflammation of the scalp to differentiate infection due to M. lanosum from that due to Microsporum audouini.

Often the history of the presence of a fungus epidemic or of the patient's contact with fungus-infected animals, living in areas endemic for certain fungi or having a systemic disease like diabetes mellitus will prove helpful in determination of the studies necessary to isolate the causative fungus.

The sense of smell may play a part in discovery of the fungus causing the eruption. In this relation, I should like to call attention to the mouselike odor of favus and the yeastlike odor of moniliasis.

Does Dr. Lewis have to apologize for a 40 per cent laboratory confirmation of his clinical impression? This excellent percentage was obtained only by taking several specimens from various sites for direct examination and culture.

The case cited by the authors in which a patient with tinea capitis no longer showed fluorescence while positive cultures were still obtainable should be emphasized to all who rely solely on the lack of fluorescence to determine cure of tinea capitis.

I would agree that the addition of antibiotics and dyes to isolation mediums is helpful but generally not necessary in the isolation of the superficial fungi, although it may be useful for that of the deep ones. It is important to reiterate that when one examines cultures of material from the nails, caution should be exercised in attaching pathogenicity to organisms generally considered saprophytic.

Research using isolation mediums containing various amounts of the amino acids has been completed by us, and the results would indicate that certain pathogens are inhibited and others enhanced by single amino acids. This observation may have practical value in therapy as well as in the isolation of single fungi where there are mixed infections.

Dr. Louis H. Winer, Los Angeles: I agree with Dr. Lewis that the staining of the fungi in the tissues is very difficult. We have recently used the Schwartz technic, but it has been unsatisfactory. It is difficult to distinguish a pathogen from a nonpathogen. In years of examining many thousands of histologic sections, we recently observed one from an ulcer on the lower extremity in which Aspergillus organisms were growing not only on the surface but also underneath the epidermis. Even though the occurrence is rare, we cannot assume that this organism is not a pathogen under certain circumstances. The observation cited marked the first time I had found the organism of Aspergillosis nigra in tissue under the epidermis.

Most frequently when we find myceliums and spores of nonpathogens they are in the stratum corneum. We cannot determine the type of organism or its pathogenicity from its appearance when seen in scales.

DR. DONALD M. PILLSBURY, Philadelphia: It has been brought out in the paper and by the discussers that there is no satisfactory method for staining fungi in tissue, at least not one which will work for many fungi. About three months ago two members of our staff, Dr. Albert Klingman, a mycologist, and Dr. Herbert Mescon, a pathologist, working with histochemical methods, found that the Hotchkiss-McManus stain visualizes fungi remarkably. This stain technic is not difficult. It depends on hydrolysis of the material by periodic acid and then treatment of it with the Schiff reagent.

The substances stained by this procedure belong in the general class of carbohydrates, such as glycogen, hyaluronic acid, gastric mucin, chitin and glycerol, which were found by Hotchkiss to give strong reactions in the Schiff reagent after periodic acid hydrolysis. Cellulose, glucose, maltose, sucrose and so forth give weaker reactions, and it is probable that in the fungi which I shall show you a polysaccharide is the material being stained. Its exact identity is being studied a little more fully at the present time.

Observations in representative slides are as follows: M. audouini; M. audouini, high power; Histoplasma capsulatum in the mouse brain, an organism which is very difficult to see with other types of stains; H. capsulatum, high power—2,000 magnification on the slide; Sporotrichum schenckii, which has never been demonstrable with in tissue previously; S. schenckii, high power [The number of forms visible with this stain are perfectly amazing to us. It seems quite likely we shall have to revise our concepts of Sporotrichum in tissues.]; Trichophyton mentagrophytes found in scrapings from human skin [This technic is not quite an office procedure as yet, although it can be done quite rapidly, in 12 to 15 minutes. It has the great advantage over the potassium hydroxide method of furnishing a permanent record, and I am quite sure that our positive scrapings with this stain will far exceed those obtainable with the routine potassium hydroxide procedure.]; Coccidioides immitis [Contrary to any reports made previously, Coccidioides does bud in tissue.]; Blastomyces dermatitidis from mouse tissue, × 2,000; Cryptococcus neoformans from mouse brain, × 400; C. neoformans, × 2,000 (I think you can appreciate the exquisite detail which is brought out by this stain); scrapings from ordinary tinea versicolor, of course easily demonstrated in potassium hydroxide scrapings but shown in much greater detail by the present method; Pityrosporum ovale, and C. albicans from an experimentally infected rabbit, material taken from the kidney.

A description of this method will shortly be published in the *Journal of Bacteriology*.

DR. GEORGE M. LEWIS, New York: My first slide is a picture of a patient with an inflammatory Trichophyton infection, and the next slide shows an adult with a Trichophyton sulfureum infection in which the diagnosis had not been made for some little time. The patient had had a scarring or at least an atrophic-looking scalp with loss of hair, and the diagnosis was finally made by culture, the Wood light examination giving negative results. I think the case illustrates a type of condition that may or may not be diagnosed for some little time.

The next slide shows an infection caused by Microsporum and reveals, again, a rather insignificant type of skin lesions; unless cultures are done routinely, one might very well miss the diagnosis.

The following slide reveals a totally different-looking skin expression due to the same organism, the first case having scaly red lesions and this, vesicular ones.

An unusual incidence but one that is not seen too infrequently, namely, a follicular infection due to T. sulfureum, is depicted in the next slide. We have encountered follicular lesions of the scalp and also of the beard, and the next slide reveals again a rather unusual T. sulfureum infection of the scalp.

The point brought out that common contaminants may occasionally become pathogenic may be illustrated by the next slide, a scraping taken from a nail showing Scopulariopsis. It illustrates the unusual association of a contaminant in tissue as a pathogen.

The following slide shows a cross section, a histologic section, showing T. crateriforme in the follicle and in the hair.

The cultures shown in the next two slides are all of the same organism, T. crateriforme, and reveal differences in the primary "isolate," illustrating the care one must take in identifying this particular organism. The first slide shows the T. crateriforme in 10 per cent dextrose agar, and the next, the same organism in a medium in which sorghum is substituted for dextrose in the same proportion, revealing the accentuation of the folds and the gross culture characteristics.

These pictures illustrate the point I made earlier, that one must become very familiar with the culture characteristics of the medium which one is using.

I wish to thank Dr. Johnson, Dr. Winer and Dr. Pillsbury for their most illuminating discussions. Dr. Johnson brought out the value of using dyes and antibiotics in certain types of culture medium for certain purposes, and I certainly agree with his concept.

Dr. Winer also mentioned the pathogenicities of Aspergillus under certain conditions, and with his comments I would agree, but, again, I would caution against the indiscriminate use of findings on primary isolation without due care. In other words, one must be very careful not to incriminate an organism as pathogenic simply because it is cultured from a disease state.

Of course, we are all greatly indebted to Dr. Pillsbury for his beautiful demonstration. My associates and I confined our paper to consideration of primary isolation in fungous infections, and I think in his discussion he certainly indicates a means for the study of the fungi themselves which we will be glad to have.

Clinical Notes

USE OF POLYVINYL ALCOHOL IN SOLUTION FOR PERMANENT MOUNTING OF FUNGI

ROBERT H. HARRIS, M.D.
LONG BEACH, CALIF.

In an attempt to produce a convenient solution for permanent mounting of fungi, I substituted an aqueous solution of polyvinyl alcohol for glycerin in a combination similar to Amaun's lactophenol as described in "An Introduction to Medical Mycology" by Lewis and Hopper.[1] Polyvinyl alcohol has been used for embedding histological specimens and has been described by several writers since 1942. Formulas similar to the one I present here have been used by others.

I have found that a preparation comprised of liquefied phenol U. S. P., 20 per cent; lactic acid sirup, 20 per cent, and an aqueous polyvinyl alcohol solution, 60 per cent, with methylene blue added for color contrast, as desired, seems to be satisfactory for making a permanent slide mount. This solution has now been tested for five months. The slide is clear, and the cover glass is attached firmly.

The method of preparation is as follows: about 20 Gm. of elvanol,® a polyvinyl alcohol of low viscosity type b, grade 70-05, obtained from E. I. du Pont de Nemours & Co., is added to 100 cc. of cold water and brought almost to the boiling point while the two substances are mixed with a spoon. The solution is then strained through gauze. The lactic acid and then the phenol are added. Methylene blue, then added for color contrast, was chosen because many dyes have an indicator effect, changing color with the p_H of the solution. Apparently the methylene blue is stable, and it is convenient to use with this acid medium.

The desired specimen is taken from a culture and placed in a drop of water on a glass slide. A sufficient amount of the mounting solution, about three or four drops, is added, and then the material is covered with the cover glass, which is pressed down with a blunt object. Clearing may be hastened by heating the preparation moderately. Thick specimens may be pressed out a few hours later when they are softer. The slide preparation takes 24 to 48 hours to harden sufficiently for the slide to be placed in a slide box.

1. Lewis, G. M., and Hopper, M. E.: An Introduction to Medical Mycology, Chicago, The Year Book Publishers, Inc., 1939.

AN UNUSUAL CASE OF MULTIPLE FUNGUS INFECTION

WILFRED E. WOOLDRIDGE, M.D.
SPRINGFIELD, MO.

Mixed fungus infections are frequent. Without question they would be found more frequently if only multiple cultures were made from persons showing various sites and types of involvement. In our experience, the mixed infection most often found is in the crural area, where an intertrigo caused by Candida (Monilia) albicans may coexist with a tinea cruris caused by a dermatophyte. It is also common to find different organisms in the crural area and on the feet in a given case. Less frequently, more than one of the dermatophytes may be obtained on cultures from the feet alone.

The following case is reported because four organisms representing three species were obtained when multiple cultures were made.

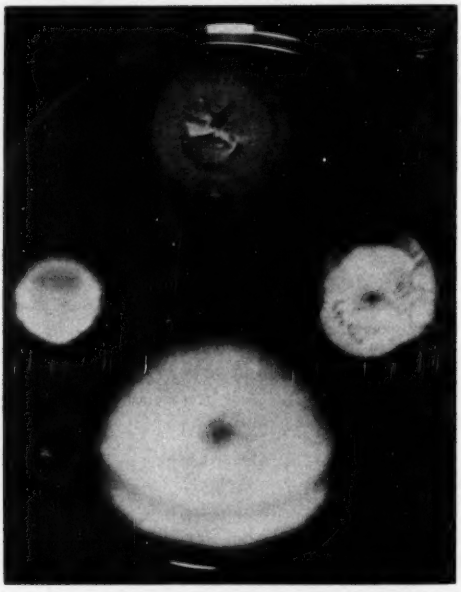
Studies, observations and reports from the Dermatological Departments of Barnard Free Skin and Cancer Hospital and the Division of Dermatology, Department of Medicine, School of Medicine, Washington University, St. Louis, service of Richard S. Weiss, M.D.

REPORT OF A CASE

F. M., a 28 year old white pharmacist, was first seen by me on Feb. 11, 1950. For the past 10 years he had regularly had "athlete's foot" during the warm weather. This would clear completely during the winter. Treatment had been sporadic and varied and continued only long enough to alleviate the symptoms of a particular attack.

During the past two years he had noted an increasing redness and scaling of the skin of the right hand, together with discoloration and dystrophy of the thumb nail of that hand. The nail involvement began beneath the free edge and slowly progressed proximally without symptoms.

At the first visit multiple cultures were made on Sabouraud's agar with scrapings taken from the right palm, from beneath the right thumb nail, from several areas around the toes of both feet and from the sole of the right foot where there was a dry, whitish scale. The left hand, left sole and the toe nails were normal in appearance.



Subcultures on a Petri dish of each of the four organisms obtained from the patient, photograph taken 11 days after inoculation (× ⅔). Top, typical Epidermophyton floccosum. Left, Trichophyton purpureum. Right, atypical E. floccosum. Bottom, Trichophyton interdigitale.

Within 10 days the culture from the right palm grew out an organism which was grossly and microscopically typical of Trichophyton rubrum. From the toes of both feet there were obtained numerous colonies of Trichophyton interdigitale. From the toes of the left foot was obtained a typical colony of Epidermophyton floccosum. From the whitish scale on the right sole there was obtained a single colony which was microscopically identified as E. floccosum but the gross characteristics of which were unusual. The accompanying figure shows the gross cultural characteristics of each of these organisms.

Treatment was initiated with 0.25 per cent anthralin cream to the right hand twice daily. The affected thumb nail was drilled free of diseased tissue with an electric drill, after which procedure a solution consisting of 2 per cent iodine crystals in benzine was applied morning and evening. For the feet, half-strength benzoic and salicylic acid (Whitfield's) ointment was applied each night with liberal amounts of zincundecate (desenex®) powder during the day.

This treatment resulted in complete clearing of the thumb nail in a period of four and one-half months. After that period the right hand was also improving and the remaining involvement was minimal. The feet promptly cleared of all apparent infection and, after unremitting treatment for another month, only the foot powder continued to be employed.

COMMENT

The isolation of four fungus organisms of three species from a single patient is distinctly unusual.

An interesting problem for speculation is whether the two varieties of E. floccosum were entirely different organisms or merely variants of the same organism, the variation being due to the different environment. This problem has been discussed by Muskatblit,[1] Wende and Collins [2] and Weidman [3] in previous publications.

Acknowledgment is made to Morris Moore, Ph.D., for his help in the study and identification of these organisms.

1. Muskatblit, E.: Observations on Epidermophyton Rubrum or Trichophyton Purpureum, Mycologia **25**:109-116 (March-April) 1933.

2. Wende, G., and Collins, K. R.: A Contribution to the Study of Epidermophyton Inguinale: Notes on an Inquiry into Morphology of Causative Fungi; Clinical and Laboratory Study of 37 Cases of Dermal Scaling, Arch. Dermat. & Syph. **3**:1-13 (Jan.) 1921.

3. Weidman, F. D.: Morphologic Variations in a Ringworm Species of the Toes Followed in Primary Cultures Over Period of Years, Arch. Dermat. & Syph. **13**:374-382 (March) 1926.

MYCOSIS FUNGOIDES WITH VERRUCOUS LESIONS

Report of a Case

NORMAN D. ASEL, M.D.
WILLIAM F. SPILLER, M.D.
AND
PAUL V. CHIVINGTON Jr., M.D.
CLEVELAND

Milian and Périn [1] in 1923 described a case of mycosis fungoides with verrucous and hyperkeratotic lesions. Jeanselme and Burnier [2] in 1926 reported two similar cases and pointed out the scarcity of reports of hyperkeratotic and verrucous lesions in mycosis fungoides. The verrucous lesions in these three cases were covered with large, thick, adherent scales. At times the lesions were dry and fissured, and they sometimes ulcerated with a serous discharge. Other manifestations of mycosis fundoids accompanied the verrucous lesions.

In the case reported herein there were exhibited no lesions of mycosis fungoides other than verrucous plaques and nodules confined to the lower extremities. Scaling and clinically evident hyperkeratosis were not present.

REPORT OF CASE

H. K., a white widow aged 63, was first seen in Cleveland City Hospital Dermatology Clinic on March 16, 1950, complaining of unsightly growths of seven years' duration on the lower extremities. The individual lesions began as small, erythematous papules which gradually enlarged peripherally, became more elevated and developed a verrucous surface. Some lesions involuted, leaving normal-appearing skin; some persisted, and an occasional new lesion appeared

From the Department of Dermatology and Syphilology, Western Reserve University School of Medicine, Cleveland City Hospital, Harold N. Cole, M.D., director, service of John E. Rauschkolb, M.D.

1. Milian, G., and Périn, L.: Mycosis fongoïde avec erythrodermie psoriasiforme et hyperkeratose végétante, Bull. Soc. franç. de dermat. et syph. **30**:394-398 (Nov. 8) 1923.

2. Jeanselme, E., and Burnier, L.: La forme verruqueuse et hyperkeratosique du mycosis fongoïde, Ann. de dermat. et syph. **7**:65-73 (Feb. 2) 1926.

Fig. 1.—Verrucous plaques on the posterior aspects of the legs and thighs.

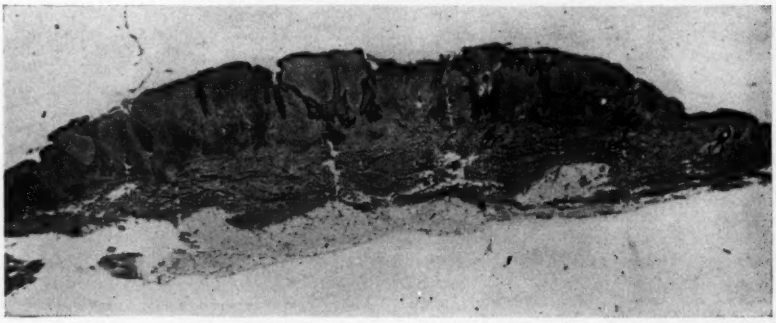


Fig. 2.—Low magnification photomicrograph showing location of cellular infiltrate and pseudoepitheliomatous hyperplasia of the epidermis; hematoxylin and eosin stain, × 4.

from time to time. The lesions were asymptomatic except for intermittent mild pruritus. No history of ingested medication was obtained on repeated questioning. Past and family history were noncontributory.

On physical examination the only abnormalities observed were about 15 well demarcated, firm, erythematous, verrucous, roughly circular plaques and nodules widely dispersed on the lower extremities. The lesions were dry and showed no evidence of scaling, crusting or ulceration. They varied from 0.5 to 14.0 cm. in diameter and from 0.2 to 1.0 cm. in elevation. There was no lymphadenopathy; the liver and spleen were not palpable.

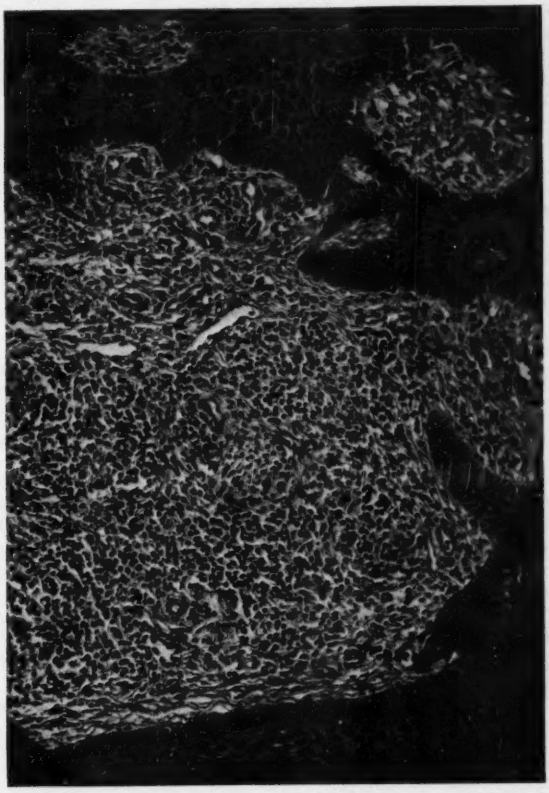


Fig. 3.—High magnification photomicrograph of cellular infiltrate; hematoxylin and eosin stain, × 100.

Laboratory Data.—The hemogram and results of urinalysis were normal. Blood Kline and Wassermann reactions were negative. Bone marrow studies revealed no abnormality. The blood bromide level was 0 mg. per 100 cc. Roentgenologic examination of the chest revealed no abnormalities other than calcification of the aortic knob.

Histological Examination.—The rete pegs of the epidermis were decidedly elongated, dipping well into the corium, and in places gave a pseudoepitheliomatous appearance. There were slight hyperkeratosis and spotty parakeratosis of the stratum corneum, which in some areas contained focal collections of disintegrating cells. The epidermis overlying the infiltrate was somewhat atrophic in some of the areas between the rete pegs. The stratum mucosum

contained a few focal areas of edema and sparse cellular infiltrate. There was mild diffuse cellular infiltration of the epidermis in some areas. The stratum germinativum was intact.

There was a rather dense cellular infiltrate occupying the upper half of the corium, giving the interpapillary areas a distended appearance. The infiltrate lay against the epidermis in some situations and in others was separated by a narrow clear zone. The infiltrate was composed mainly of small cells with round, deeply staining nuclei and larger cells with paler staining elongated nuclei which contained irregular granules of chromatin. Both types showed a tendency toward indentation of their nuclei and pronounced variation in size and shape. The deeper staining cells varied considerably in staining quality and showed a tendency toward clumping. Mitotic figures were rarely seen.

Numerous blood vessels in the upper part of the corium were dilated and considerably hyperplastic.

Treatment.—A short trial course of stibanose® (the diethylamino-ethanol salt of sodium antimony gluconate; 1 cc. contains 20 mg. of antimony), 4 cc. intramuscularly twice weekly, was given for a total of nine injections. No improvement was noted, and the patient was then given roentgen ray therapy using the following factors: 90 kv., 5 ma., 25 cm. distance and 0.5 mm. Al inherent filtration with no added filtration. The total dose to each individual lesion was 600 r, given 150 r weekly for four doses. Improvement was pronounced, and the lesions disappeared, leaving residual hyperpigmentation.

MICROSPORUM AUDOUINI ISOLATED FROM A DOG

THOMAS W. MURRELL Jr., M.D.
RICHMOND, VA.

Tinea capitis due to Microsporum audouini is believed by most investigators to be transmitted from man to man or indirectly from clothing or furniture contaminated with infected hairs.

REPORT OF A CASE

In February 1949, we observed a 7 year old boy presenting areas on the scalp clinically suggestive of tinea capitis due to M. audouini. The areas of semibaldness or broken hairs were fluorescent to examination with Wood's light. Cultures were positive for M. audouini.

The mother was emphatic in her belief that the patient had not come in contact with a child known to have tinea capitis. The patient was the only child in his school found positive on Wood light examination, and no child in the immediate neighborhood was known to have the disease. The mother suggested that her fox terrior might be the source. The dog was examined and was found to have circinate eczematous lesions on the jaw, below the mouth. Wood light examination revealed an area of typical fluorescence, and from this area multiple cultures were made. Typical growth of M. audouini grossly and microscopically appeared in 12 days. These cultures were recultured and examined at the Medical College of Virginia (Reed) and Duke University (Conant), studies at both places confirming the diagnosis obtained in our laboratory.

SUMMARY

A case is reported of a dog as an unquestioned carrier of M. audouini. It is suggested that dogs may be sources of infection in tinea capitis due to M. audouini as well as in that due to M. canis. It may be possible that dogs acquire the disease from man and transmit the disease to children.

17 East Grace Street (19).

Society Transactions

CHICAGO DERMATOLOGICAL SOCIETY

Theodore Cornbleet, M.D., President

James R. Webster, M.D., Secretary

March 15, 1950

Branchial Cyst? Presented by Dr. T. Cornbleet and (by invitation) Dr. H. Schorr and Dr. D. Musgrave.

DISCUSSION

Dr. M. R. Caro: I agree with the diagnosis of branchial cyst. I think that the lesion should be removed because squamous cell carcinoma has been reported as developing in some of these lesions many years later.

Myoblastoma. Presented by Dr. T. Cornbleet, Dr. D. Cohen and (by invitation) Dr. D. Musgrave.

J. W., a 52 year old Negro woman, first noticed a small dark nodule starting in the region of the left anterior axillary fold 13 years ago. This has very slowly enlarged until now it represents a very hard, infiltrated lesion, approximately 2 cm. by 1.5 cm., with a hyperpigmented warty surface which is bound down to the underlying tissue.

About four years ago the patient noticed a fulness in the left supraclavicular region, and about one year ago a definite subcutaneous nodule was noticed in this area.

DISCUSSION

Dr. F. R. Schmidt: Examining this section with the low power magnification I was struck with the observation of closely packed groups of cells which did not have a definite outline. Many of us thought at first that they were xanthoma cells. They looked as though they contained mucin. Mucin has been reported in many of these tumors. I would say, without having studied the section at length, that this lesion might be a granular cell myoblastoma but that it is in an early stage. Grouping has not taken place, and formation of the granules is incomplete.

Dr. Sture Johnson: Madison, Wis.: There is a firm, freely movable tumor in the left supraclavicular area on which biopsy should be done, since it may represent a metastasis, which is rare for myoblastomas.

Dr. M. R. Caro: This lesion is a granular cell myoblastoma. It is not of the densely packed cellular type that we have presented here several times, but with the Van Gieson stain many granular cells were demonstrable. Because the nodule is large and somewhat invasive I think that it should be excised very widely and sections run on the different parts to see whether there is a malignant change in any portion. The enlarged cervical nodes should also be removed and examined.

Acrosclerosis. Presented by Dr. H. Rattner, Dr. H. Rodin and (by invitation) Dr. D. Musgrave.

Acrosclerosis. Presented by Dr. J. Webster, Dr. S. Bluefarb and (by invitation) Dr. D. Musgrave.

DISCUSSION OF THE PRECEDING TWO CASES

Dr. W. Kurt Wiener, Milwaukee (by invitation): I call attention to the pronounced hippocratic (longitudinally curved) nails, which I have seen in another case of acrosclerosis.

Dr. F. R. Schmidt: I want to report the treatment for scleroderma which we have used at the Marine Hospital. Some of the members might try it. We use an infusion of 0.1 per cent

procaine hydrochloride. Each treatment consisted in the administration of 500 or 800 mg. at three day intervals. We have two cases in which there has been considerable improvement. When one patient came in he could not flex his fingers and he had a cardiac embarrassment. He has made a very remarkable recovery objectively. After a few treatments he has been able to flex his fingers and is very much more comfortable.

Diffuse Symmetric Lipomatosis ("Fetthals," Madelung); Cirrhosis of the Liver. Presented by Dr. J. Webster, Dr. S. Bluefarb and (by invitation) Dr. S. Barsky.

S. G. is a 56 year old Austro-American man who first noted the onset of nontender cutaneous masses on his chest about four years ago.

The patient states that the skin tumors appear to recede at times and have never caused him any discomfort or inability to perform his work.

For the past three years he has felt quite weak, and he has noted a weight loss of approximately 100 pounds (45 Kg.) during that time.

He has drunk about 1 pint (473 ml.) of whisky daily for the last 20 years.

He was recently admitted to the hospital because of an auto accident in which he sustained a laceration of the left side of the forehead with third nerve paralysis, fracture of the left fibula and cerebral concussion with unconsciousness. Physical changes consisting in retrograde amnesia, confusion and anxiety noted in the hospital cannot easily be attributed to either the accident or the syndrome or both.

No history of similar skin lesions or of any mental disorders is recalled for any other member of the patient's family.

On physical examination, the patient is observed to be a pale, asthenic man who presents numerous nontender subcutaneous soft, fleshy, movable masses over his neck, trunk and upper extremities. The hands, distal portions of the forearms, lower extremities and upper regions of his head are apparently free of lesions. Many dilated veins are seen coursing over the affected parts.

Both eyes appear exophthalmic. The left eye is exotropic; the left pupil is large and does not react to light.

The liver border is felt 10 cm. below the right costal margin in the midclavicular line. The spleen is moderately enlarged. There is bilateral inguinal adenopathy. Pronounced varicosities are present on both legs.

Dr. Sture Johnson, Madison, Wis.: "Fetthals," according to Lyon (*Arch. Int. Med.* **6**:24-120, 1910) is associated with pain which may be spontaneous or induced by pressure. This is not present in this case, although the other characteristics, i. e., symmetry, diffuseness and typical location of the lipomas, are present. I feel that the term "Fetthals" should be limited to use for those cases having painful nodules over the joints.

Dr. Stephen Rothman: This patient actually has Madelung's disease. Painful lipomas or adiposis dolorosa is a different entity.

Dr. Samuel M. Bluefarb: Adiposis dolorosa (Dercum's disease) is characterized by abnormal fat deposits which may be nodular or diffuse and associated with tenderness over the affected areas as well as neuralgic pain and asthenia. On the other hand, diffuse symmetric lipomatosis consists of fatty masses which are not circumscribed or encapsulated but diffuse and symmetrically distributed. In the large majority of cases the neck is the part especially affected, the "Fetthals" of Madelung thus being produced, although other parts are usually involved to some extent. Unlike other forms of lipomatosis, the condition occurs chiefly in males.

Sarcoidosis with Uveitis. Presented by Dr. M. H. Ebert, Dr. V. Leaf and (by invitation) Dr. S. Barsky.

DISCUSSION

Dr. M. H. Ebert: This case was very interesting because there was some discussion as to whether or not sarcoidosis is a relatively benign disease. My associates and I have seen at Cook County Hospital a reasonably large number of cases of sarcoidosis. This is the first one I recall where there was such a pronounced involvement of the eye. While this man still can distinguish light from darkness, to all intents and purposes he is blind. One can hardly speak of sarcoidosis in his case as being benign when it leaves the patient blind. It is a question how much good the treatment has done.

At the annual meeting of the Minnesota Dermatological Society, Dr. Michelson presented a youngster with minor skin lesions and with eye involvement. He said that in reading the German literature he found that it was suggested that fever treatment would result in amelioration not only of the eye condition but also of the sarcoidosis in general. We proposed in the present case to give the patient a series of fever treatments, as much as he can stand, and see whether that therapy would have any effect on the sarcoidosis. I am quoting Dr. Michelson at length because I have not seen the original article. According to his statement, a German physician in Bonn had a patient with sarcoidosis that was refractory to treatment. The man acquired a febrile disease, and the lesion healed.

DR. M. C. SPENCER, Danville, Ind. (by invitation): Recently Dr. Ralph Jones at the Hospital of the University of Pennsylvania has been treating a small series of cases of sarcoid with urethane. I am sure he will report his observations soon. His dose varies from 2 to 4 Gm. a day. It is necessary to follow the patient carefully doing weekly white blood cell counts. The

Acrodermatitis chronica atrophicans associated with hyperthyroidism.

treatment is given on an ambulatory basis. Certainly this method of treatment is worth considering, and the results are quite dramatic.

This method of treatment was discovered accidentally on the medical ward. During testing of the toxicity of urethane one of the patients with pulmonary sarcoidosis was sent to the roentgen ray department a week after the urethane therapy was started. There was such a dramatic change in the lung picture in the roentgenogram that the physicians concerned wondered whether they had made a mistake. They subsequently followed up testing with other patients and confirmed the result and the effectiveness of the administration of urethane in the treatment of pulmonary sarcoidosis as well as other manifestations of this disease.

DR. STEPHEN ROTHMAN: Sarcoidosis is certainly not a benign disease in the Negro or in the white race. Not only may patients go blind from uveitis but also they often die from rapidly progressing pulmonary fibrosis. Those who live may be seriously incapacitated.

It might be interesting to note that 20 to 25 years ago all cases of sarcoid-uveitis were diagnosed as "tuberculous iritis." Apparently there is no such disease at all. If the tubercle bacillus invades the eyeball, as it often does in lupus vulgaris, the eye is soon lost because panophthalmitis develops.

Acrodermatitis Chronica Atrophicans and Hyperthyroidism. Presented by Dr. Stephen Rothman and (by invitation) Dr. Esther Farney-Davies.

DISCUSSION

Dr. Bernard Yaffe (by invitation): There was a recent report from Sweden of the cure or improvement of over 50 cases of acrodermatitis chronica atrophicans with intensive penicillin therapy; not only were the inflammatory lesions resolved but also the atrophy disappeared in this series.

At the February meeting of this society Dr. M. H. Ebert and I presented a classic case of acrodermatitis chronica atrophicans with large active inflammatory patches in addition to the characteristic atrophy. In view of the Scandinavian report this patient was given over 8,000,000 units of penicillin intramuscularly, without any improvement being noted.

Dr. Stephen Rothman: The recently suggested penicillin therapy certainly did not work in this case. The unilateral involvement is remarkable. This patient had acrodermatitis for 30 or 40 years. Her thyroid disease developed much later.

Dr. H. Rattner: There have been three such cases presented before this society in recent years. The old teaching was for one to look for a syphilitic background in cases of unilateral acrodermatitis chronica atrophicans.

Sjögren's Syndrome Associated with Lymphoblastoma and Hypersplenism. Presented by Dr. Stephen Rothman and (by invitation) Dr. Matthew Block and Dr. Fred V. Hauser.

D. G., a 49 year old housewife, has had burning and dryness of her eyes and blurring of vision since 1923 and a very dry mouth since 1935. In 1939 she had influenza, and subsequently arthritis of the fingers, ankles and knees. She has had "strep" throats every winter since then, and in 1947 she had erysipelas of the face. She has had numerous swellings of the submaxillary and parotid glands, sometimes associated with salivary calculi; in 1946 a swelling of the right parotid gland broke through the skin. In the same year she had a mastoidectomy on the right side. In 1942 she was told that her spleen was enlarged and that she had no "acid in her stomach." She has been taking liver and iron for anemia for many years. Over the last 10 years her skin has become thin and very dry and she has had hemorrhages into the skin. A splenectomy was performed in December 1949.

On physical examination she is observed to be a thin, chronically ill white woman. Her skin is very dry and atrophic with prominent veins and many telangiectasias. Scalp, axillary and pubic hair is very sparse. Brown mottled pigmentation is present over both legs. The eyes appear sunken because of the loss of orbital fat. There are vertical rows of dilated veins on the lids. The palpebral and bulbar conjunctivas are injected. There is much sticky mucus on the cornea. Staining with fluorescein showed many punctate erosions. The tear secretion test gave very low results.

There is generalized atrophy and dryness of the mucous membranes of the ears, nose and throat. The lips are dry and cracked at the corners. The tongue is a ruby red color. There is petechial hemorrhage of the soft palate, nasal septal perforation and bilateral nerve type deafness.

Pronounced enlargement of the left parotid and a mass of nodes in the left post cervical chain are observed. These swellings have subsided a great deal since roentgen ray therapy. There is a large mass of lymph nodes in the left axilla.

The liver is down 2 or 3 fingerbreadths. Prior to splenectomy the spleen was palpable 4 fingerbreadths below the costal margin.

There is enlargement of the second and third metacarpal phalangeal joints, and contractures of elbows are noted.

In laboratory work, roentgenograms of the skull revealed calcific deposits inside the calvarium in the left frontal-parietal region (tuberculoma?). There was left frontal sinusitis. Examination of the chest and gastrointestinal tract revealed normal conditions. The urine gave a reaction for albumin and had a 3 to 5 red blood cell count per high power field and a 3 to 5 white blood cell count. Urea clearance was 30 per cent of normal. Nonprotein nitrogen was 34 mg. per 100 cc.

Postoperative blood counts showed hemoglobin, 14.8 Gm. per 100 cc.; red blood cell count, 4,040,000, and white blood cell count, 4,300, with 76 per cent neutrophils, 1 per cent eosinophils, 1 per cent basophils, 19 per cent lymphocytes and 3 per cent monocytes. The bleeding time was normal, the clotting time prolonged and the clot retraction normal. There were 293,800 platelets. The Rumpel-Leede test showed slight capillary fragility.

Liver function tests showed severely impaired function. The cephalin flocculation reaction was 3+, and thymol turbidity, 3+; in the sulfobromophthalein test there was 20 per cent retention (normal, 5 per cent). Serum bilirubin was 0.2 mg. (direct) and 0.5 mg. (indirect) per 100 cc. Total plasma proteins were 5.5 Gm., with 3.7 Gm. of albumin and 1.8 Gm. of globulin per 100 cc. Total cholesterol was 155 mg. per 100 cc., with 105 mg. in esters form. Results of the glucose tolerance test were normal. Gastric analysis revealed very few drops of secretion and no free acid. Biopsies of liver, spleen, bone marrow and lymph node revealed a picture of lymphoblastoma with features of Hodgkin's and reticular cell sarcoma. Treatment has consisted in closure of both tear ducts, splenectomy (Dec. 1, 1949) and roentgen ray therapy to the left parotid and cervical regions. A section of a lymph node biopsy specimen is presented.

The lymph node biopsy specimen showed the normal lymph node architecture completely obscured by an overgrowth of dense lymphatic tissue. The dominant cell present was a large, hypertrophic, bizarre-appearing multilobate reticular cell. Mitoses and degeneration were frequent. There were no eosinophils or typical Sternberg-Reed cells, but there was a diffuse scattering of small lymphocytes. A similar lesion was found in the marrow, spleen and liver. The diagnosis was Hodgkin's sarcoma or reticular cell sarcoma.

DISCUSSION

DR. ROBERT KIERLAND, Rochester, Minn.: Sjögren's syndrome is one with which dermatologists for the most part are not familiar. It has been the problem of ophthalmologists for many years because of the keratitis sicca which is part of the syndrome. My own interest was aroused some two years ago by Dr. J. W. Henderson, one of my colleagues in ophthalmology. We noted that a great proportion of these patients had a dry asteatotic skin and many had keratosis pilaris. Accordingly, vitamin A, both by mouth and intramuscularly, was given to some of these patients with good results, both as far as improvement being shown in skin manifestations and dryness of the mouth and also in that there was increased tearing.

DR. STEPHEN ROTHMAN: I should like to ask Dr. Kierland whether the cases he saw were associated with systemic disease, as seen in this patient.

DR. ROBERT R. KIERLAND, Rochester, Minn.: It seems that the associated condition of lymphoblastoma would be coincidental rather than part of Sjögren's syndrome itself.

DR. MATTHEW BLOCK (by invitation): This patient was first seen presenting a very unusual condition consisting of a desiccation of all the mucous membranes of her head. She also had anemia, leukopenia and thrombopenia. Trying to put the whole picture into one classification seemed very difficult. We thought she had Sjögren's syndrome and hypersplenism, with the latter possibly secondary to some type of lymphoblastoma. The patient had her spleen removed, with complete recovery as regards her hematological status. About two months after operation she manifested what we thought was a swelling of the parotid gland with fever, malaise and loss of appetite. She had experienced this with arthritis on two previous occasions. Below the parotid gland was a lymph node, which on biopsy was observed not to show the picture of Hodgkin's sarcoma. Similar lesions were found in the bone marrow, liver and spleen. Probably Sjögren's syndrome has nothing to do with the lymphoblastoma.

Pseudoatrophoderma Colli. Presented by DR. SAMUEL J. ZAKON and DR. AARON L. GOLDBERG (by invitation).

An Italian-American girl aged 25, in good health, states that in the past two years she has acquired an eruption on the neck and upper portion of the chest. The lesions are non-inflammatory, and there are no subjective symptoms. Various forms of topical therapy have had no influence on the lesions.

On superficial examination the eruption gives the appearance of a pigmentary disturbance in that some of the lesions are vitiligo-like and surrounded by a zone of hyperpigmentation.

Thus the skin of the neck is given a retiform appearance. The vitiligo-like lesions appear atrophic. However, on close examination the depigmented areas, especially those on the upper portion of the chest, appear glossy. The entire pattern fades when patient stretches the neck.

Studies of potassium hydroxide preparations were negative for fungi, and there was no visible fluorescence under the Wood light.

DISCUSSION

DR. S. W. BECKER: I believe this girl presents a picture described several years ago by Dr. Muir and me. The skin is not atrophic; it simply looks atrophic. In at least one instance of this disorder complete recovery has taken place.

DR. SAMUEL J. ZAKON: I want to thank Dr. Becker for confirming the diagnosis. It is interesting to note that Dr. Becker did not include this rare clinical entity in his book but that it is in Dr. Ormsby's book.

Amyloidosis Cutis (Secondary?) of Legs. Presented by DR. E. LIEBERTHAL.

DISCUSSION

DR. STURE JOHNSON, Madison, Wis.: It is my feeling that this patient has primary and not secondary amyloidosis. Recently a patient with generalized amyloidosis involving the tongue as well as the skin has been treated by us with ACTH. There has been pronounced improvement in that the myxedema-like changes in the hands, face and tongue have subsided, permitting the patient to wrinkle the skin and to whistle. The urine has been very highly colored, suggesting that porphyrin-like bodies might be present. Further studies are now in progress.

Dr. Scharrenberg, a neuropathologist at the University of Michingan, has called my attention to the role that roentgen rays may play in the causation of amyloid deposits. He has studied the surgical specimen of the brain of a patient who came into the hospital with observations and symptoms of a tumor of the frontal lobe of the brain. This person had received, years earlier, 10,000 units of roentgen rays for a basal cell carcinoma of the skin immediately overlying the area of the brain in which the amyloid tumor was found. Similar cases have been reported in the German literature. Roentgen ray therapy probably should be added to the list of causes for amyloid disease.

DR. M. R. CARO: Was there something in the history about this patient's having been treated for syphilis some years ago?

DR. T. CORNBLEET: He was treated with bismuth for tabes dorsalis.

DR. M. R. CARO: That fact might point to the primary source of his amyloidosis.

Granuloma Following Injury from Fluorescent Light Bulbs(?). Presented by DR. CLEVELAND J. WHITE.

DISCUSSION

DR. M. H. EBERT: Some months ago Dr. Ormsby and I presented photomicrographs of a beryllium granuloma, though we did not present the patient. Our patient injured his skin with a fluorescent bulb, and the microscopic picture was similar to the one shown today. The characteristic picture is numerous small foci of epithelioid cells, giant cells and some lymphocytes with surrounding fibrous tissue. The difference, as Dr. Becker pointed out, between beryllium granuloma and sarcoidosis is the fact that beryllium granuloma breaks down and becomes necrotic while ordinary sarcoid does not. I thought histologically this case was a good example of beryllium granuloma.

DR. MATTHEW BLOCK (by invitation): In the various areas of the atomic bomb project there have been several accidents among the personnel working with beryllium. The only way to incriminate beryllium is by examination of the urine or organs for beryllium. Attempts are being made to determine what is a normal or abnormal liver content of beryllium. My associates and I have seen a few cases, and histologically it is impossible to separate some

of the lesions from sarcoid or some of the types of caseating granulomas unless the causative organism or chemical substance is demonstrated. It is very hard to make a pathological diagnosis other than sarcoid or a sarcoid-like lesion by the histopathological picture of the granuloma alone.

DR. M. R. CARO: At the round table of histopathology at the Academy we presented several cases of beryllium granuloma. The histological picture in them was identical with the one shown today.

DR. M. H. EBERT: The question is a little out of order, but I should like to ask Dr. Block, because he has had considerable experience with beryllium, whether or not every person who gets a fragment of beryllium in the skin acquires a granuloma. That question was brought up by Dr. Hass. The disorder is so much like sarcoid that he believed that most people who get those fragments did not acquire beryllium granuloma.

DR. MATTHEW BLOCK: My experience is limited. I happen to be friendly with some of the people who work on beryllium. I do not know about skin injuries due to fragments. These persons I referred to have very carefully worked out determinations of the concentration of beryllium in the air and tried to correlate the concentration with the development of single lesions in various patients, as well as with the development of generalized granulomas. There is no strict correlation between this concentration and the development of beryllium granulomas systemically. There have been some patients working where there was a very high concentration in the air who did not manifest berylliosis. Other patients in the same area and in the same circumstances acquired a generalized type of the disease. The diagnosis is proved by demonstration of an abnormal amount of beryllium in the urine and in the tissues.

DR. A. L. WELSH: My associates and I have been interested in beryllium granulomas for some time. There is one building in Cincinnati in which eight floors have no windows. All illumination is accomplished with fluorescent lights. Two of the maintenance men in this building had injuries from broken fluorescent tubes. One had five injuries, and the other two, and neither of them acquired any granulomas. Accordingly Dr. Hass's opinion may have some value.

Pigmented Purpuric Lichenoid Dermatitis (Gougerot and Blum). Presented (by invitation) by DR. M. C. SPENCER, Danville, Ill.

Dermatological examination reveals over the extensor surfaces of both feet and both ankles confluent plaques of dusky red papules; extending from ankles to midthighs are patches of discrete erythematous papules which on diascopy do not blanch completely. The eruption is remarkably symmetric.

The prussian blue reaction was positive. A discrete papule was seen on routine hematoxylin and eosin staining. Hyperkeratosis and parakeratosis were seen. The basal layer was intact. Round cell infiltration was prominent in the papule only. The vascular tree was not unusual, but perivascular round cell infiltration was present.

In neurological consultation Dr. Jordan's observations consisted in (1) paresthesias of a "numb-cold-heavy feeling" in both legs (2) absent ankle jerks and barely perceptible knee jerks; (3) absent vibratory sensation to the third lumbar dermatome and (4) swaying on the Romberg test (no disturbance of cerebellar or position senses).

DISCUSSION

DR. ROBERT R. KIERLAND, Rochester, Minn.: It seems unfortunate that there are so many names ascribed to a condition which is a simple purpura and hemosiderosis. While I do agree with the diagnosis as presented, I would also agree if the diagnosis had been presented as one of Schamberg's disease or angioma serpiginosum. In other words, those three conditions are basically the same entity, a condition due to a manifestation of increased capillary permeability or fragility. The reason for the capillary injury, however, remains obscure in most patients. The examinations of the peripheral blood reveal normal values and lack of bleeding tendencies. Many of these patients will have improvement in their condition with the administration of rutin and vitamin C.

DR. S. W. BECKER: If I am not mistaken hemosiderosis is not seen in angioma serpiginosum.

DR. ROBERT R. KIERLAND, Rochester, Minn.: I do not think it makes much difference. Hemosiderosis is frequently seen in many purpuric lesions when the biopsy specimen is taken from the lower extremities, but a similar type of lesion fails to show hemosiderosis when the specimen is taken from the upper part of the trunk and upper extremities. In other words, biopsy specimens may be taken from the same patient in two different locations, and one will show hemosiderosis and the other will not.

DR. S. W. BECKER: I think all these conditions are due to capillary fragility, but I think the ordinary conception of hemosiderosis is different. We have all seen legs with brownish to blackish discoloration following stasis ulcer or varicose veins. I think that Schamberg's disease and the disease of Gougerot and Blum of which the patient presents a typical example are very closely related. I do not think this disorder is just a stasic hemosiderosis; it occurs in areas where there is no stasis.

DR. STEPHEN ROTHMAN: I agree with Dr. Becker that stasic dermatitis due to varicose veins can easily be differentiated from this entity. On the other hand I agree with Dr. Kierland that it is highly problematic whether Schamberg's and Gougerot's diseases are true entities. They all are purpuric diseases of the leg. In most instances it is impossible to establish the cause of such purpura. In this case, however, it might be related to the tabes of the patient. He states that the purpura was preceded by severe paresthesias in the legs.

DR. A. H. SLEPYAN: During the second world war a great number of men were seen at the hospital with the picture of purpura of the lower extremities, at times simulating Schamberg's disease and at times the picture of Gougerot syndrome. On questioning of these men it was discovered that all had had infections of the upper respiratory tract a week to 10 days prior to the appearance of the eruption. As a rule they were new recruits and had been doing a considerable amount of marching. After several months the entire process would clear regardless of treatment. It is most likely that we were dealing with a toxic manifestation with injury to the capillaries of the lower extremities on an orthostatic basis.

DR. MATTHEW BLOCK (by invitation): I have not seen very many cases. Similar to Dr. Kierland's experience, we were unable to demonstrate any signs of generalized bleeding. The results of the prussian blue test for iron were rather disappointing, since some forms of iron in the tissues will not give a positive reaction. As I understand, in this case there was no positive reaction to the test for iron. In the cases in which there is not a positive reaction one may demonstrate the iron by spectroscopic analysis or by means of microincineration.

DR. M. C. SPENCER, Danville, Ill. (by invitation): I appreciate the discussion. I do want to make a correction. Dr. Caro looked at the section stained with prussian blue, and in his opinion the reaction was positive for iron.

The primary reason for presenting this case was the symptoms that the patient has recently manifested in the last few months, i. e., paresthesias, absent knee jerks and almost complete absence of the ankle jerks, with loss of vibratory sensation to the third lumbar dermatome. We still occasionally see such problems in syphilis, and I wonder whether or not we cannot make the diagnosis of tabes here despite the fact that the reactions to spinal fluid tests and serologic tests for syphilis have been negative. The patient had a history of gonorrhea 20 years ago but denies any genital or extragenital lesions. He is one of those unusual persons in this day and age who have never received penicillin. I think he deserves a course of penicillin despite the negative results of laboratory studies.

Pellagra(?). Presented by DR. H. RATTNER, DR. H. RODIN and (by invitation) DR. D. MUSGRAVE.

Acute Disseminated Lupus Erythematosus. Presented by DR. H. RATTNER, DR. H. RODIN and (by invitation) DR. D. MUSGRAVE.

Lupus Vulgaris. Presented by DR. H. RATTNER, DR. H. RODIN and (by invitation) DR. S. BARSKY.

Ulcer of the Cheek: Previous Treatment of Basal Cell Epithelioma with 6,000 R. Presented by DR. T. CORNBLEET, DR. D. COHEN and (by invitation) DR. S. BARSKY.

Folliculitis Ulerythematosa Reticulata. Presented by DR. H. RATTNER, DR. H. RODIN and (by invitation) DR. S. BARSKY.

Papulonecrotic Tuberculid and Erythema Induratum. Presented by DR. F. E. SENEAR and Staff.

Multiple Benign Cystic Epithelioma Involving Nose and Ears but Not Eyelids. Presented by DR. M. R. CARO.

Pemphigus Vulgaris? Pemphigus Erythematosus? Presented by DR. CLEVELAND J. WHITE and (by invitation) DR. F. R. SCHWARTZ.

BRONX DERMATOLOGICAL SOCIETY

Charles R. Rein, M.D., *Vice President, in the Chair*

Henry Silver, M.D., *Secretary*

March 16, 1950

Larva Migrans. Presented by DR. JULIUS H. POLLOCK.

E. C., a boy aged 2 years, presents an eruption on the right foot which has persisted and extended to date. The mother states that the rash appeared about six weeks ago during their stay in Florida.

On the anterior portion of the right foot, mainly on the plantar surface, there is a linear lesion which tends to encircle the foot almost twice and crisscrosses at several points. Much of the lesion is flat and gives the appearance of a burrow with collapsed walls accompanied with pigmentation and scaling. However, near the ball of the large toe there appears to be the active end of the lesion with definite burrow formation, edema, redness and pustulation.

DISCUSSION

DR. ABRAHAM J. ORFUSS: Following the suggestion of Dr. Dobes, I have treated at the Skin and Cancer Clinic two cases of larva migrans with poultices of bermuda onion. Both cases completely cleared within one week.

DR. EMANUEL MUSKATBLIT: I would suggest freezing the lesions with ethyl chloride spray.

DR. MARTIN V. BOARDMAN: I am not in favor in the use of antimonials in this disease. They are, in my opinion, potentially harmful for use in so limited an infestation. We know the eruption to be self limited, although we cannot put an exact time on the course. But, since the Ancylostoma exists in the larval form and is incapable of reproduction, time, if nothing else, will eventuate a cure. Therefore, I suggest a simple and purely local therapy, whether it be the use of freezing by either solid carbon dioxide or ethyl chloride or the application of an antiseptic ointment to prevent secondary infection.

DR. DAVID B. BALLIN: Since this is a self-limited disease and the host is in no particular jeopardy from the parasite, why not leave it alone?

DR. ALEXANDER A. FISHER: While it is true that practically all cases of larva migrans from Florida are due to the Ancylostoma larvae, it must be remembered that in other parts of the country the horse botfly, Gastrophilus, may cause a form of larva migrans which is indistinguishable from the larva migrans presented tonight.

DR. JULIUS H. POLLOCK: About four years ago I had under my care a patient, a plumber, who, while installing a water unit under a beach bungalow at a Florida resort, became massively infested with larvae of Ancylostoma. He must have had at one time as many as 100 to 150 larvae over the trunk and extremities. He remained under my care for the next 10 weeks, and I was afforded an excellent opportunity to note the character of the migration of the larva. Some observations I made pertain to the discussion tonight.

With regard to antimony, I began treatment of the patient at the time Dr. Smith had just introduced the use of this remedy in larva migrans. I used stibophen (fuadin®) for four weeks, and I noted the best effect I could achieve with the drug was a cessation of the activity of the larva rather than a larvicidal effect. In addition, I found that there appeared toxic manifestations from the antimony in the doses necessary to control the larva.

As to topical application, it would be hard for anyone to mention any parasiticidal substance that I omitted to use, all without benefit. I did not know about bermuda onion poultice at the time. The only treatment with which I had steady but slow results was the use of ethyl chloride. I used some 60 tubes of 10 Gm. each during the time the patient remained under my care. Solid carbon dioxide snow was used by me on several occasions, but the reaction was severer than that with ethyl chloride and that method was not a convenient modality in such an extensive case. Even with the use of ethyl chloride the treatment was a difficult, painful and laborious one.

Although the textbooks lead one to believe that it is a simple procedure to pick the larva out of the burrow, doing so is far from easy, since the larva wanders about in any direction and

crosses over its burrow at many points. At the end of 10 weeks there was a large nidus in the scrotal skin which necessitated hospitalization. With a local spray of ethyl chloride while the patient was under general anesthesia, the remaining nest of larva disappeared.

It seems to me that the observations recorded in the literature on "creeping eruption" are often inadequate. For one thing, I do not believe that the larva perforce dies if left alone over a period of two or three weeks. The case shown tonight also demonstrates this point. The larva may remain quiescent for a while and then start migrating again. In my patient I was able to note that burrows would develop at distant sites where previously there had been no such lesions for weeks. Therefore, I think that the larva can travel in some other manner than merely through the corneal layer of the skin. Interestingly enough, my patient had Loeffler's syndrome with fever, eosinophilia, cough and abnormality observed on roentgenologic examination of the lungs.

Lichen Planus et Acuminatus Atrophicans (Lichen Planopilaris). Presented by Dr. Nathan Sobel.

M. M., a woman aged 42, was previously presented by the late Dr. E. W. Abramowitz with the diagnosis "folliculitis decalvans associated with lichen spinulosus" on Jan. 13, 1942, at the Manhattan Dermatological Society (Arch. Dermat. & Syph. **45**:1182 [June] 1942) and on April 7, 1942 at the New York Academy of Medicine (Arch. Dermat. & Syph. **46**:899 [Dec.] 1942).

The patient was discharged from the Skin and Cancer Clinic on June 19, 1942. After that time she was perfectly well until January 1950, when there developed an itchy eruption on the chest and back which spread rapidly. The patient returned to the clinic on March 10, 1950.

On the chest, upper part of the back, abdomen, inguinal and genital regions and thighs there are shiny reddish papules the size of a pinpoint or pinhead, some showing distinct umbilication. Many lesions, particularly those on the shoulders, are follicular papules with grayish, horny spines. On the flexor surface of the forearms there are diffuse plaques formed by coalescence of lichen-planus-like lesions. The buccal mucosa shows numerous whitish papules the size of a pinpoint or pinhead, in addition to fine reticulated streaks. On the abdomen there are a few broken bullous lesions which suggest impetigo contagiosa. The scalp shows total alopecia and is atrophic. The nails show longitudinal striations and are dry and brittle.

DISCUSSION

Dr. Wilbert Sachs: Nine years ago I expressed the opinion that this patient would eventually manifest lesions of lichen planus. Subsequently, Dr. Bloom presented the case as typical lichen planus. The lesions on the scalp are lichen planopilaris.

Dr. Julius H. Pollock: At the last meeting, I presented a case of lichen planus et acuminatus atrophicans. Dr. Umansky objected to the diagnosis for the reason that clinical lesions of lichen planus were absent. He maintained that their presence was absolutely necessary in the formulation of a diagnosis of lichen planus et acuminatus atrophicans. The case presented this evening is proof that lichen planus lesions may be absent at times in the course of the disease. This observation has been noted by others.

Another interesting point about this case is the extensive alopecia. While patches of atrophy may coalesce, such an extensive alopecia as that in this case has not been described in connection with this disease. The atrophy, especially in the absence of lichen planus lesions, cannot be differentiated from that seen in other atrophic diseases of the scalp.

Dr. Henry Silver: The point raised by Dr. Pollock regarding the presence or absence of lichen planus lesions in this disease is well taken. There is nothing to indicate folliculitis decalvans in this case. It is true that in lichen planus et acuminatus atrophicans, alopecia has not been reported to be as extensive as in this case. The atrophy, as a rule, is superficial, sometimes even in the form of pseudoatrophy as it appears on the skin following the resolution of lichen planus patches. Dr. W. Sachs demonstrated that point clearly in his study (Arch. Dermat. & Syph. **45**:1081-1082, 1942).

DR. EMANUEL MUSKATBLIT: I have seen such smooth atrophy and alopecia in favus which lasts for many years. In this case I would not hesitate to make a mycologic examination to exclude the possibility of fungi being present there. The other disease which will produce such smooth progressive alopecia and atrophy is alopecia cicatrisata or pseudopelade. I do not think that lichen planopilaris causes such smooth scarlike atrophy.

DR. WILBERT SACHS: Both pseudo and real atrophy are seen in the presented case. I recall Dr. Rein's patient at the Skin and Cancer Clinic in whom complete alopecia developed in the course of many years.

DR. FRANZ H. HERRMANN: It appears of interest that this patient clearly states that she "hardly" perspires, as is especially obvious to her during the warm season, when "everybody else" sweats profusely. She has noticed this condition for the past 17 years, since her last pregnancy. She is so averse to high temperature in summer that she feels unable to leave home because she would experience attacks of headache, dizziness and palpitations and be on the verge of fainting. These are the symptoms of the sweat retention syndrome described by Dr. M. Sulzberger and co-workers *(J. Invest. Dermat.* **9**:221, 1947). A study of the response to experimentally increased environmental temperature, of the degree of sweat delivery to the skin surface, would be interesting in this case. Likewise, investigation of serial sections of an excised lesion, as well as of a specimen from an uninvolved site, is suggested, since plugging of the sweat pores seems likely to be encountered.

A therapeutic attempt with large doses of vitamin A appears of promise. Moreover, periodically enforced sweating may be helpful. Twenty-two years ago, K. Kuerst and I obtained, and published an account of, excellent curative effects in lichen planus, which effects resulted from frequent exposures to dry heat (*Dermat. Wchnschr.* **88**:397, 1927). I have attained this result frequently since that time.

DR. NATHAN SOBEL: Dr. Sachs was right when he contended from the study of the histological slides in 1942 that this patient would go on to acquire typical lichen planopilaris. The alopecia in this case is much more extensive than that usually seen in this disease.

Myxedema Tuberosum Circumscriptum of the Legs. Presented by DR. CHARLES F. SIMS and DR. HANS H. BIBERSTEIN.

L. G., aged 38, Chinese, was operated on for toxic goiter on March 2, 1948. Preoperative examination by his physician, Dr. V. Fanoni, disclosed pronounced tremor, with a pulse rate of 120, a systolic murmur, weight of 94 pounds (42.6 Kg.) and a basal metabolic rate of + 64. Examination of the blood showed 5,000 erythrocytes and 5,800 leukocytes. The Wassermann reaction of the blood was negative. The patient received sedatives, digitalis, propylthiouracil and strong iodine solution for 10 days preceding the operation. After the thyroidectomy, at which a small part of the gland in the upper portion of the left lobe was left, there was uneventful recovery. The basal metabolic rate went down to + 8 and the pulse rate to 70.

In November 1948, after six weeks' of medication with propylthiouracil, bluish thick "spots" began to appear on the anterior surfaces of the legs. The medication was discontinued immediately, and the patient was referred to the Skin and Cancer Clinic.

On the legs there are raised infiltrated large nodular lesions. The region of the eyebrows shows slight alopecia and some swelling. The ulnar nerves are not thickened. A keloidal scar indicates the site of the thyroidectomy.

The basal metabolic rate was 2 per cent below the average normal. The amounts of cholesterol and the total proteins as well as the albumin/globulin ratio and the sedimentation rate were within normal limits. Examination of the urine showed no abnormal condition. A nasal smear for Hansen bacilli was negative, as was the Wassermann reaction of the blood. Examination of the blood showed 100 per cent hemoglobin, 4,900,000 red cells and 5,000 white cells with 45 per cent polymorphonuclear cells, 3 per cent eosinophils, 2 per cent basophils, 40 per cent lymphocytes and 10 per cent monocytes.

Histological examination showed an acanthotic epidermis and slight hyperkeratosis. The basal margin contained pigment cells. The collagen fibers were separated. The mucin cells showed granules of a red-violet color and stellate shape, with threads projecting from the cells. The histological diagnosis was myxedema.

DISCUSSION

DR. MAURICE UMANSKY: It seems that circumscribed myxedema is not due directly to hyperthyroidism. It occurs for the most part in patients after the thyroidectomy, with a situation similar to that with exophthalmos, which develops oftener after than before thyroidectomy. It is known that exophthalmos is apparently due to a disturbance of the pituitary gland. In the last two to three years it was found that exophthalmos responds readily to administration of radioactive iodine. For that reason it may be well worth while to use radioactive iodine in the case presented.

DR. ARTHUR B. HYMAN: Dr. Umansky, is of course, correct in his opinion that exophthalmos is closely related to circumscribed myxedema and that both are due to edematous infiltration of the tissues. This infiltration is obviously not caused by increased thyroid secretion, since it is present though the thyroid has been removed. Furthermore, the patient has been given propylthiouracil, which treatment in a sense results in a medical thyroidectomy. Exophthalmos and the localized myxedema are both due to anterior pituitary hormone disturbance, and there is no purpose in administering radioactive iodine. Vilanova and Canadell (*J. Clin. Endocrinol.* **9**:883-894, 1949), in an article on circumscribed myxedema, reported on the treatment of two cases with estradiol benzoate, in one case with excellent results and in the second with much improvement.

DR. HANS H. BIBERSTEIN: First, I want to add one more fact which was not mentioned in the history. When the patient extends his tongue, he does so incompletely, with its tip bending downward, because of swelling and induration. Doessekker and Reitman made similar observations (*Arch. f. Dermat. u. Syph.* **123**:76, 1916). I think our discussion showed how necessary it is to read old literature. Some of the suggestions made today correspond to therapeutic procedures used in the first cases of this condition described some 40 years ago. At that time there was no idea of the role of the pituitary gland, but a thyroid preparation was tried by Doessekker and sodium iodide gave a good result in the case of Lewtschenkow (*Monatsh. f. prakt. Dermat.* **50**:6, 1910). Furthermore, in the case of Doessekker (who, by the way, suggested the name myxedema tuberosum) two implantations of thyroid gland tissue (removed from a patient with Graves' disease) into the bone marrow cavities of the tibias gave excellent results: all the manifestations underwent involution within a few weeks to a few months after the operations. Doessekker already considered the possibility that it might not be the thyroid gland alone which is responsible for the disease and the curative effect of his substitution therapy, but factors determined by other endocrine glands.

A Case for Diagnosis: Paget's Disease of the Scrotum? Presented by DR. FRANCES PASCHER and DR. CHARLES F. SIMS.

H. S. C., a man aged 43, registered at the Skin and Cancer Unit of University Hospital of the New York University-Bellevue Medical Center on Feb. 7, 1950, presenting a lesion of five years' duration. He gives no history of previous cutaneous disorders. His general health has been good. He was treated until April 1946 with 20 weekly roentgen ray exposures without any effect on the lesion.

The patch began with a reddish chafed area the size of a half dollar, associated with burning and itching. It did not enlarge for about five years and never entirely regressed. Several times a year it appeared as if it were healing, taking on a more or less shiny appearance. Then suddenly it would become rough and oozing again, with denudation of small areas of skin, making it appear as if it had been scratched. For the past four months the lesion has been extending proximally.

On the lateral surface of the scrotum is a well defined slightly raised and infiltrated, 4 by 2 cm. oblong patch. It is pear shaped, with the base below and the upper pole narrowed to about 1 mm. and bent on itself. The latter portion is the part that has extended during the last four months. On the surface are pinpoint-sized and slightly larger pitted marks which appear excoriated. The lesion is somewhat moist, painless and nontender. There are no enlarged inguinal lymph nodes. There is a slightly raised, moderately infiltrated reddish patch the size of a pea on the outer side of the right ankle, of several months' duration.

The Mazzini test reaction was negative. Examination of the urine showed no abnormality. The hemogram was normal except for the observation of 3,600 leukocytes and 14 per cent monocytes.

The histological examination by Dr. C. F. Sims showed an irregular and acanthotic epidermis. Several patchy areas of parakeratosis were seen. The chief point of interest, however, was the rete cells, which in many areas of the prickle cell layer had become dyskeratotic. The cells were large; the swollen prickles appeared lost, and the cytoplasm was pale and delicately reticulated. The nuclei were large, oval, round or semilunar and deeply staining. Many mitotic figures were present. There were some multinucleated cells. There was a moderate inflammatory reaction in the upper part of the cutis consisting of round, plasma and wandering connective tissue cells. The histological diagnosis was Paget's disease (?).

DISCUSSION

DR. WILBERT SACHS: Microscopically, this is a classic case of Bowen's disease.

DR. CHARLES WOLF: As I recall it there are recorded cases of Paget's disease which present essentially dry plaques. This case would seem to be such an example. The fine distinction microscopically, of whether the disorder is Bowen's or Paget's disease, is a question of different interpretation of the cells by the pathologist.

DR. ARTHUR B. HYMAN: Paget's disease of the scrotum must be rare, and we have no evidence of a deep carcinoma, such as has been found in the apocrine glands in association with Paget's disease of the axillary skin or in the rectum with Paget's disease of the anus, to parallel the observations in the breast with Paget's disease of the nipple. The lesion is dry and histologically is a pagetoid type of Bowen's disease, a diagnosis which could hardly be made with ease. The histological criterion for Paget's disease is the Paget cell, which is large, has light-staining cytoplasm, loses its prickles and becomes separated from the surrounding cells. As a result of this process, one often finds in sections round or oval empty spaces in the epidermis, from which the affected cells have fallen out in preparation of the slide. In this case we have many groups and a large number of cells with clear cytoplasm, closely resembling Paget cells, but they adhere to each other and to the surrounding cells and leave no empty spaces. On the other hand, there are smaller groups of cells, not so conspicuous, which have all the variety of shape, size, staining reaction and type of nucleus which is associated with Bowen's disease. Darier pointed out that, though low in the epidermis one finds binucleate or trinucleate Paget cells in Paget's disease, as the surface of the skin is reached the cell loses all but one nucleus. The multinucleated Paget-like cells here can be seen at all levels. I agree with Dr. Sachs that we are dealing with a case of Bowen's disease, but hardly with a typical one.

DR. PERRY M. SACHS: The patient has an early suspicious lesion on the leg which clinically has the picture of Bowen's disease more than that of Paget's disease.

DR. WILBERT SACHS: In the slide I did not find the typical larger basal cell which is so characteristic of early Paget's disease.

DR. RUDOLF L. BAER: Some years ago Dr. Sulzberger and I had under our care a case similar to the one presented. The eruption was located in the groin and extended to the scrotum. It was more superficial but moist in appearance, showing an extremely fine infiltrated border. Clinically we suspected Paget's or Bowen's disease, and histologically the lesion was found to be Paget's disease. Subsequently the entire lesion was excised and that operation followed by plastic repair. The patient has remained well now for four years.

DR. FRANCES PASCHER: Dr. Maurice N. Richter, who also studied the slides, agreed that the altered cells were indistinguishable from Paget cells. Intracellular bridges were absent; the majority of the cells were unicellular, and some were multinucleated. We do not feel that the presence of multinucleated cells excludes the diagnosis of Paget's disease, since Ormsby has described them and Dr. C. Sims found multinucleated cells in a number of cases of Paget's disease of the nipple. This observation is based on a study of 25 mammary cases.

Osteoma Cutis; Result of Treatment for Acne Scarring. Presented by DR. MORRIS LEIDER.

L. L., aged 40, presented herself for treatment of scarring from acne of many years' duration. About 30 weekly treatments with a chemical caustic (trichloroacetic acid) and cryotherapy (carbon dioxide "slush") were administered. The osteomatosis was discovered on roentgen ray examination.

DISCUSSION

DR. FRANZ H. HERRMANN: It is remarkable that these inorganic deposits as sequelae in certain cases of acne escaped attention until Dr. Leider's recent report. Since osteoblasts were demonstrable, one can hardly doubt that there is ossification. However, in vitro tests, carried out repeatedly with some of the calcified, egg-shaped particles, which Dr. Leider kindly left with me for investigation, would not lead to the conclusion that this material is bone. It dissolved relatively fast in tenth-normal hydrochloric acid solution, under escape of carbon dioxide. Only a trace of apparently organic matter, which was enclosed in concentrically arranged shells of the inorganic concretion, remained. A spot test for calcium gave a strongly positive reaction. One should conclude, therefore, that the particles consist chiefly of calcium carbonate. Ordinary bone behaves differently in vitro.

DR. EMANUEL MUSKATBLIT: I was interested to hear from Dr. Herrmann the results of his chemical studies of these deposits. If not bone structure chemically and if not calcium phosphate but calcium carbonate then the condition cannot be called osteoma. It is something which simulates bone tissue and is an osteoma-like condition but not osteoma.

Osteoma cutis.

DR. CHARLES WOLF: We have examples in the human body of formations from the separation from serum of various chemicals. We have those deposits in the gallbladder, kidney and urinary bladder, which are calculi, and the formations in the present case may be skin calculi as a result of skin irritation and chemical change interacting with sebaceous gland secretions after long inflammatory reaction.

DR. MORRIS LEIDER: Dr. Herrmann's in vitro studies with the tiny osteomas which I gave him suggest that they are composed almost entirely of calcium carbonate, whereas comparative analysis of skeletal bone shows much less of this salt. In my original case (ARCH. DERMAT. & SYPH. **58**:168, 1948), whence came the specimens which Dr. Herrmann worked with, I had qualitative chemical microanalysis performed and calcium phosphate was reported too. Of course it is quite possible that these abnormally situated and abnormally developed bones are somewhat different in composition from true bone. This idea does not detract from the histological evidence that the condition is one of true bone formation rather than some form of simple calcinosis. However, Dr. Herrmann tells me that French writers do not make a distinction between calcinosis and ossification. Apparently eventual invasion with osteoblastic and osteoclastic elements is to be expected when calcium is deposited in more than average amounts. Finally, Dr. Herrmann's cautious suggestion, based on the microscopic appearance of the decalcified residue, that the osteomas may be calcified or ossified mites—Demodex folliculorum would be the organism—is startling. The objections to this possibility are that the osteomas are situated in the midcutis and that they are not related to sebaceous glands or pilosebaceous ampullae and orifices.

I wish to refer to the treatment of acne scarring especially since only recently an elaborate method by sandpaper abrasion was described (*J. A. M. A.* **142**:647, 1950). Unfortunately I do not have before and after photographs in my present case, but I can assert that the therapy changed this patient's appearance from extreme ugliness to the present acceptable aspect. The method used—which is not original—consisted in weekly applications of 100 per cent trichloroacetic acid to all the high points of the scarred skin followed immediately by gross over-all refrigeration with solid carbon dioxide powdered and slushed with acetone. The treatment is painful but can be made tolerable by application to the acid-treated areas of cotton pledgets soaked with cold water and by initial gentle application of the refrigerant until numbness permits more carefree pressure. The patient's fortitude and cosmetic aspirations plus the operator's skill and experience are factors in determining the number of treatments and length of time required for a reasonable result.

A Case for Diagnosis: Lipoma of the Left Index Finger? Presented by DR. ABRAHAM J. ORFUSS.

A. P., a woman aged 27, states that at the age of 10 years she had a "very large wart" on the left index finger, which was not treated and disappeared spontaneously. At about the same time she noted that her finger began to enlarge and grew at a steady slow rate to its present size. The patient thinks that the finger is turning sideways from the pressure of the growth. There never was associated pain, bleeding, loss of weight or systemic symptoms. No other member of the family of eight siblings presents this growth. There is no history of injury to the finger.

The entire left index finger is considerably enlarged. On the medial aspect there are soft subdermal lobulations of varying size. They are not tender to the touch, lack any signs of inflammation and do not interfere with flexion of the finger.

Roentgenologic examination of the left index finger showed generalized swelling of the soft tissues of the palmar aspect. There is dorsal deviation and subluxation of the terminal phalanx. Sharp osteophytes are noticed at the lateral margins of the opposing aspects of the terminal and middle phalanges. All other fingers showed no abnormalities. The impression is that there are swelling of the soft tissues and subluxation of the terminal phalanx associated with osteoarthritis.

DISCUSSION

DR. CHARLES WOLF: Was a diagnostic puncture done? I believe from the clinical appearance and on the basis of palpation and other sensory reactions I received from examination that that we are dealing with a lymphangioma or lymphangiectasia. We should employ aspiration puncture to determine whether mucinous fluid or serum can be obtained. I do not think the disorder is lipoma.

DR. RUDOLF L. BAER: It seems to me that the changes are not only in the soft tissues. If one compares the size of the index fingers and the nails on both sides one can see that there is a considerable difference. There must be some involvement of the structures other than the soft tissues. Have roentgenograms been taken of the cervical part of the spine to rule out a cervical rib?

DR. JULIUS H. POLLOCK: May I suggest the use of transillumination to help differentiate between a solid growth and a cystic or purely vascular or lymphangiomatous tumor? This procedure would also be of help in therapy.

DR. ABRAHAM J. ORFUSS: In answer to Dr. Baer, no roentgenologic examination of the cervical part of the spine was made; this will be done. I have not as yet aspirated the mass, as I wanted to get a clinical impression as to what was suspected. The radiologist suggested an angioma rather than lipoma.

Nevus Linearis Tardus. Presented by DR. GEORGE KLEIN and DR. IRVING D. EHRENFELD.

Lupus Miliaris Disseminatus Faciei. Presented by DR. NATHAN SOBEL.

A Case for Diagnosis: Lichen Striatus? Presented by DR. JOSEPH L. MORSE.

A Case for Diagnosis: Nevus Linearis? Lichen Striatus? Presented by DR. IRVING D. EHRENFELD.

Macular Atrophy. Presented by DR. DAVID B. BALLIN.

Multiple Symmetrical Nevi of the Face. Presented by DR. HANS H. BIBERSTEIN.

A Case for Diagnosis: Congenital Cyst? Supernumerary Mamma? Presented by DR. JOHN GARD.

Chronic Radiodermatitis of the Face, with Epitheliomatous Degeneration. Presented by DR. ABRAHAM J. ORFUSS.

METROPOLITAN DERMATOLOGIC SOCIETY

Joseph C. Amersbach, M.D., *President*
Valentine C. Baker, M.D., *Secretary*
March 20, 1950

Acrosclerosis. Presented by Dr. Leslie Paxton Barker.

M. K., a 51 year old Negro woman, three years ago noticed a gradual onset of stiffness of her fingers. This has gradually become more noticeable and has extended to a stiffness and tightness of the skin of both forearms. Within the past few months she has noticed a tightness and stiffness of the face. For three years prior to the present illness the patient noticed coldness and numbness of the fingers, especially noticeable after exposure to cold. These symptoms have increased with the progress of the stiffness and tightness of the skin.

The patient had a hysterectomy for pelvic tumor in 1941.

There is tightness and sclerosis of skin over the fingers with partial flexure of most fingers and inability to straighten them; the skin is shiny and appears almost transparent; the fingers are cold. The sclerosis extends up the forearm, gradually fading into normal skin at the elbows. There is moderate tightness and sclerosis of the skin of the face but not of the neck. The feet appear normal.

A blood count showed 74 per cent hemoglobin and 4,000,000 red blood cells. The white blood cells and differential count were normal. Results of urinalysis were normal and the electrocardiogram was normal. The sedimentation rate was 54 mm. per hour. The Wassermann reaction was negative. Blood urea was 7.1 mg. per 100 cc. A roentgenogram of the lungs showed some parenchymal fibrosis in both lower lung fields with thickening of the pleura in both apexes. A roentgenogram of the hands revealed fragmentation and absorption of the distal tufts of the right third, fourth and fifth digits. There were some osteoarthritic changes in the interphalangeal joints and slight demineralization of the bones in general.

The patient has been given alpha tocopherol, 50 mg. three times a day, iron and liver by mouth, hot soaks and massage for the hands and arms.

DISCUSSION

Dr. Thomas N. Graham: I agree with the diagnosis.

Dr. Royal M. Montgomery: I would give vitamin E both intramuscularly and orally. In one case I have been following there were no remarkable results but the acrosclerosis was improved.

Dr. Valentine C. Baker: What about using vitamin D? Sodium thiosulfate is sometimes helpful in these cases.

Dr. J. Lowry Miller: The history and observations are typical of acrosclerosis. The lack of involvement of the feet is not unusual. The prognosis in this case is good. There is involvement of the fingers which might even lead to gangrene, but the patient will live a long time. The differential diagnosis is between scleroderma with sclerodactylia and acrosclerosis.

Dr. Leslie Paxton Barker: I think there is a definite syndrome of acrosclerosis that differs from generalized scleroderma. In acrosclerosis the sclerotic changes begin on the hands or feet and face simultaneously, and the process progresses in a symmetric fashion. The skin changes are accompanied with, or preceded by, local syncope and asphyxia and are accompanied with pain in cold weather similar to the symptoms seen in Raynaud's syndrome. An interesting feature in this case is that the symptoms began shortly after a hysterectomy.

Sarcoidosis. Presented by Dr. Valentine C. Baker.

B. H., a Negro aged 35, three months ago noticed lesions on the left wrist, both antecubital spaces and the dorsum of the left hand at the base of the index finger.

Ten years ago, in Jacksonville, Fla., the patient had a similar eruption all around his neck, on his eyelids and with a number of discrete lesions on his arms. The lesion on his neck began as a small papule and gradually spread to involve his entire neck. He received three to four

roentgen ray treatments to the neck only. The lesions pained slightly and began to heal in 1943, leaving scars. No lesions were present from 1943 until three months ago. The patient's general health is good. He had epitrochlear nodes excised 10 years ago.

Examination of the neck showed spotty hyperpigmentation and atrophy with large keloids on the back of the neck. The arms showed numerous scars, which the patient stated were at the sites of previous lesions. New lesions consisted in coin-sized papular plaques with no erythema, vesiculation or lichenification.

The Wassermann reaction was negative. The sedimentation rate was 25 mm. per hour. The reaction to the tuberculin test, with a dilution of 1 : 100,000, was negative, as it was with a dilution of 1 : 10,000. A roentgenogram of the hands revealed no abnormalities. Chest roentgenograms showed infiltration in both upper lung fields with slight enlargement of hilar nodes. The biopsy showed sarcoidosis.

DISCUSSION

DR. J. LOWRY MILLER: I accept the diagnosis. This is an interesting case because of the amount of atrophy around the neck and arm. There is a history of roentgen ray treatment but a lack of other features of radiodermatitis. I do not believe roentgen irradiation to be the cause of the atrophy. Sarcoid does heal with atrophy in certain cases. A biopsy of one of the small lesions at the edge of the neck should show the histologic picture of sarcoid.

DR. LESLIE PAXTON BARKER: I think this case of papular sarcoid is very unusual because of the retiform type of scarring that has occurred in bandlike fashion around the neck.

DR. WILLIAM M. HUBER: I agree with Dr. Miller. I do not believe that the roentgen ray treatments have produced the atrophy in this case. If the atrophy were due to roentgen rays it would follow a geometric pattern, which it does not. The atrophic areas, on the other hand, appear in discrete localizations, as if they represented the sequelae of antecedent papular lesions. There have been many reports in the literature of atrophy following sarcoid lesions. Dr. Gerald F. Machacek recently presented a case before the New York Academy of Medicine in which widespread macular atrophy of the Schweninger-Buzzi type apparently followed sarcoidosis.

DR. CARL T. NELSON: I agree that the skin lesions of sarcoid in the Negro may show atrophy during the process of involution. When this occurs the patient is left with glazed, depressed scars which may persist for a long time. Regarding the roentgen ray treatment of cutaneous sarcoid, I cannot say that I have ever seen a case in which I could convince myself that such therapy was beneficial.

DR. VALENTINE C. BAKER: I did not know how to explain the keloid on the neck. I think it must be of traumatic origin. I am inclined to think the atrophy of the lesion on the neck is due to roentgen ray exposure.

Panniculitis; Erythema Induratum? Presented by DR. LESLIE PAXTON BARKER.

E. C., a 40 year old Negro housewife, acquired a painless, firm red nodule on the inner aspect of the left calf. The lesion has increased slightly in size and has no subjective sensation. The patient had fusions of the spine for tuberculosis in 1944, 1945, 1946 and 1947 and in September 1949 was operated on for tubercular salpingitis.

The inner aspect of the left calf has a red, subcutaneous, infiltrated lesion about 2 inches (5 cm.) in diameter. It is quite well circumscribed and attached to the skin but is freely movable on the subcutaneous tissue. It is only slightly tender.

A roentgenogram of the lung revealed no active tuberculosis. A complete blood count and determinations of blood urea, uric acid and cholesterol were all normal.

DISCUSSION

DR. WILLIAM M. HUBER: The tissue sections showed pronounced vasculitis and panniculitis. These features would be consistent with a diagnosis of erythema induratum. No tuberculoid infiltration was present, however. Not much of the tissue of the hypoderm was included in the sections. Had the biopsy gone deeper it might have been possible to say definitely whether or not the condition is erythema induratum.

DR. CARL T. NELSON: Admittedly the short duration of these lesions is somewhat against a diagnosis of erythema induratum. Nevertheless, this patient has a definite past history of tuberculosis and the present lesions are compatible with a nodular, necrotic type of tuberculid.

DR. THOMAS N. GRAHAM: Clinically this eruption appears to be erythema nodosum. The nodules are tender and have the distribution seen in erythema nodosum. The acute onset also suggests this diagnosis.

DR. ROYAL M. MONTGOMERY: This case is more typical of erythema nodosum.

DR. J. LOWRY MILLER: I think this is a panniculitis but not nodular nonsuppurative panniculitis. The lesion is too large for erythema nodosum. One lesion is unusual for erythema induratum. I thought first of morphea and then of panniculitis. If the lesion heals and leaves a depression this development will be more definite evidence of panniculitis. The biopsy did not go deep enough to show the characteristic pathologic picture of panniculitis. The size of the lesion and the fact that it healed so quickly are against erythema induratum.

DR. LESLIE PAXTON BARKER: When I first saw this patient she had a bright red, deep-seated, infiltrated lesion of doughy consistency that could have been panniculitis, erythema nodosum or tuberculosis of the hypoderm. The lesion has improved so much during the last few days that I think it is probably erythema nodosum even though there is practically no tenderness.

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Baltimore-Washington Dermatological Society, Host

March 25, 1950

Ainhum? Presented by DR. RAYMOND C. VAIL ROBINSON, Baltimore.

D. A., a Negro girl aged 5 months, had the onset of constrictive bands of the fingers and toes shortly after birth. There was no swelling of the affected fingers or toes at any time.

Involving the left thumb and middle, ring and little fingers and the right middle and little fingers near the proximal portion there are narrow constrictive bands which are quite deep. Similar bands are on the first two right toes and the left middle toe. The fingers and toes are warm, and there is no evidence of atrophy.

DISCUSSION

DR. BERNARD APPEL, Boston: I think that these are congenital constrictive bands from uterine developmental changes. Roentgenologic studies should be made to see whether there are any changes in the bones. In two cases that my associates and I saw in Boston several years ago, in adults, there were bone changes.

DR. HARVEY BLANK, Philadelphia: Ainhum begins on the plantar surfaces. It does not begin at birth and is found in the tropics. The present case, I think, is one of congenital constrictive bands.

Eosinophilic Granuloma. Presented by DR. FRANCIS A. ELLIS, Baltimore.

This case was reported by Dr. Fred Weidman (ARCH. DERMAT. & SYPH. **55**:155 [Feb.] 1947.).

DISCUSSION

DR. WALTER F. LEVER, Boston: I believe that the term eosinophilic granuloma should be limited at present to two types of cutaneous lesions: one type is a variant of Hand-Schüller-Christian disease and associated with eosinophilic granuloma of the bone; the other type is characterized by purple patches on the face. These two types of eosinophilic granuloma represent two entirely different diseases.

DR. WILBERT SACHS, New York: It is not entirely clear that these large endothelial cells are from the blood vessels, and, if they are, this condition would never be a granuloma. There are many eosinophils present in this section, and, rather than create a new term, I think that we should study further the possibility of the origin of some of these cells.

DR. HERMAN BEERMAN, Philadelphia: I agree with Dr. Lever rather than Dr. Sachs in regard to the possible origin of these so-called endothelial cells. There is no question that in the granuloma in some of these vascular-like structures there are red cells. I believe with Dr. Lever that they are vascular spaces.

DR. FRANCIS A. ELLIS, Baltimore: Most pathologists with whom I have discussed this case agree that the lesion is primarily a vascular tumor. Wherever specimens are taken of the patient's tissue or cells, as from lymph nodes, from the bone marrow or the blood stream there are so many eosinophils in the lesion as secondary. In other words, the eosinophils are there because they are everywhere. It is not unusual, where there are sweat glands in a lesion, that these show hyperplasia of the epithelial cells, as may be present in this biopsy specimen.

Chronic Discoid Lupus Erythematosus, Limited to the Lips. Presented by DR. ISRAEL ZELIGMAN, Baltimore.

DISCUSSION

DR. FRANCIS P. MCCARTHY, Boston: Clinically the condition does not suggest lupus erythematosus. Lupus erythematosus about the lips usually begins in the skin and, by continuity, involves the lips. The condition cleared up when the patient was on a vacation in Bermuda and exposed to the sun. The onset of the lip condition was acute and not what one would expect in a case of lupus erythematosus.

DR. ISRAEL ZELIGMAN, Baltimore: My diagnosis is based on clinical grounds, because of the sharp delimitation of the involved area, with telangiectasis, scaling, erythema and edema.

ADDENDUM.—After 14 weeks of treatment with bismuth subsalicylate in oil once weekly, the eruption completely cleared up. Dr. Lloyd W. Ketron saw the histological picture and stated that lupus erythematosus was a very distinct possibility in this case.

Acrokeratosis Verruciformis (Hopf); Acanthosis Nigricans (Juvenile Type) of Axillas. Presented by DR. ISRAEL ZELIGMAN, Baltimore, and DR. CHARLES SHERTER (by invitation), Veterans Administration Hospital, Fort Howard, Md.

DISCUSSION

DR. ISRAEL ZELIGMAN, Baltimore: This patient has had some flat wartlike lesions on the hands, ankles, wrists and forearms as long as he can remember. They would appear to be flat warts on visual examination, but microscopically they are observed to be localized areas of hyperkeratosis and acanthosis. One also sees similar localized and more extensive hyperkeratotic areas, namely, keratosis palmaris et plantaris and knuckle pads. In addition, the patient has mild acanthosis nigricans of the axillas, which condition I believe is completely unassociated with the acrokeratosis verruciformis.

Lichen Simplex Chronicus of the Glans Penis. Presented by DR. MARK HOLLANDER, Baltimore.

The patient was presented before the Baltimore-Washington Dermatological Society in October 1949. Diagnoses offered ranged from vegetative dermatitis through tuberculosis verrucosa cutis to a precancerosis and epithelioma. Treatments suggested varied from watchful waiting through local destructive measures to amputation of the penis.

DISCUSSION

DR. FRANK C. COMBES, New York: I think the whole clinical picture in this case can be explained on the basis of irritation, both from infection and also from manipulation, the latter to a great measure by the patient himself at other times as well as on the application of medication prescribed by his various physicians. I think there is also a psychoneurotic problem

here that should not be overlooked. The infection I mentioned may be the direct result of this manipulation, or it may be reflex. I recall two similar cases; in one there were about a dozen vesical calculi which were asymptomatic, and in the other there was a prostatic calculus. The vegetative balanitis disappeared on the removal of the stones in both instances.

Dr. Francis A. Ellis, Baltimore: I think the lesion is primarily hyperkeratosis with secondary infection. I would advise amputation because I think this is a precancerous lesion.

Dr. Mark Hollander, Baltimore: In view of his emotional problems, I doubt that the patient would submit to amputation. One must take into consideration the genesis of this condition. There was phimosis, with purulent subpreputial exudation, constantly for two years, at the end of which time circumcision was done and the infection was more or less cleared up. The patient was left with the present lesion on the glans. This lesion received much treatment with grenz rays during November and early December and showed excellent response while under treatment. It has relapsed slightly since treatment was discontinued. Dr. Combes's suggestion about urinary calculus will be investigated. My own feeling is that the condition is etiologically on an emotional basis, but I am not at all sure what to do for the patient.

Scleroderma: Acrosclerosis. Presented by Dr. Mark Hollander, Baltimore.

DISCUSSION

Dr. Frank C. Combes, New York: Acrosclerosis belongs to that group of diseases sometimes referred to as the nitrogen storage dermatoses. Dr. Co-Tui and I have consistently found a negative nitrogen balance in scleroderma. On its correction by administration of concentrated proteins we have observed improvement both subjectively and objectively. In no instance, however, have I observed a complete remission. The significance of this negative balance is unknown to me.

Dr. Maurice J. Costello, New York: At the present time my associates and I have a patient under ACTH treatment, and the result up to this point after a period of one week is not short of remarkable. In reference to the discussion just made here by Dr. Combes, the protein intake of the patient was increased by giving large doses of proteins up to 6 to 8 ounces (170 to 227 Gm.) a day. There was a marvelous improvement in the condition.

Dr. Frank E. Cormia, New York: I think that the last discussion by Dr. Costello is very interesting, particularly with relation to the remarks of Dr. Combes. With ACTH therapy, a negative nitrogen balance is the rule. I wonder whether Dr. Combes would like to comment on this fact, especially as it pertains to the case under discussion.

Dr. Frank C. Combes, New York: I am sorry, but I have had no experience with ACTH other than with its use in two patients with subacute lupus erythematosus (*Proc. Soc. Exper. Biol. & Med.* **72**:563-565, 1949).

Dr. Walter F. Lever, Boston: I have participated in the treatment by ACTH of four patients with diffuse scleroderma (Bayles, T. B.; Stout, C. F.; Stillman, J. S., and Lever, W. F.: The Treatment of Scleroderma with Adrenocorticotrophic Hormone: Preliminary Observations, in Mote, J. R.: Proceedings of the First Clinical ACTH Conference, Philadelphia, Blakiston Company, 1950, p. 447). During the treatment there was moderate clinical improvement: tightness of the skin and dysphagia decreased, and there was improved mobility of the joints. But the improvement was merely temporary. Within two or three weeks after cessation of therapy the patients were in the same condition as they had been before treatment. Skin biopsies made at the beginning and at the end of therapy showed no change. In regard to Dr. Combes' remarks about nitrogen balance, I should like to mention that ACTH tends to increase urinary nitrogen excretion and thereby produces a negative nitrogen balance.

Dr. Neville Kirsch, Hartford, Conn.: If there is a nitrogen protein deficiency and a negative balance, I should suggest a trial of testosterone. I feel it would at least help reverse that situation, which I believe has been reported by John Lane of Oklahoma and Swartz of Boston.

COMMANDER WILLIAM C. MARSH, Bethesda, Md.: In relation to ACTH, we have a drug available at Bethesda called doca,* desoxycorticosterone acetate, which we give in 5 mg. doses. So far as we know, we have had no side reactions. This drug is given in oil, and its use is followed in two to five minutes with the administration of 0.5 to 1 Gm. of ascorbic acid intravenously. It is being given with excellent results and without any of the side effects of ACTH.

DR. MAURICE J. COSTELLO, New York: We have treated a group of cases as discussed by the previous speaker, and we haven't had such excellent results at all; some six or seven years ago we treated a number of patients at Bellevue Hospital, and during that period it seems to me the patients manifested a disorder of the heart. That was our main reason for discontinuing treatment. I think that possible development should be kept in mind.

DR. GEORGE E. MORRIS, Boston: Let me reemphasize what Dr. Costello has said, about desoxycorticosterone acetate. This was used in treatment of patients with pemphigus, and 12 patients seemed to be helped and were discharged from the hospital. This work was done in 1941; subsequently four patients died while on this same treatment. At the time of treatment I wrote a paper about the use of this substance, but I have kept it in my files since these four patients died. One should be most careful about what one writes about these chemicals. Such reactions are not side reactions but rather straightforward metabolic reactions caused by the chemicals, and the use of these substances must be carefully controlled.

DR. DONALD S. MITCHELL, Montreal, Canada: In regard to the protein balance, after the use of ACTH, one of the noticeable effects in a case treated in the hospital in Montreal was the change from a negative protein balance to a positive one.

Schweninger-Buzzi Type of Primary Macular Atrophy; Multiple Benign New Growths of the Skin. Presented by DR. MARK HOLLANDER, Baltimore.

J. T., a 32 year old Negro woman, first manifested the lesions 13 years ago and feels that there has been no change at all since then. There was no antecedent skin disease, and there have been no subjective symptoms at any time. There is no history of syphilis.

On examination may be seen oval, wrinkled, pale, raised lesions which feel quite flabby and which disappear on pressure. The examining finger seems to push right through the lesions into the subcutis but the lesions reappear promptly on the release of pressure. They behave much like herniations of the subcutis through the cutis. These lesions are present predominantly in the axillas and over the chest, back, upper arms and neck.

Blood serologic tests for syphilis gave negative reactions.

On microscopic examination the epidermis seemed to be slightly atrophic although the rete pegs were moderately well developed. There was a mild dilatation of capillaries in the upper part of the cutis surrounded by a very light mantle of infiltrate. The connective tissue stain showed coarse large bundles of darkly staining collagen in the midcutis and lower portion of the cutis. Some of these changes were artefacts due to incomplete decolorization.

Fibroxanthoma. Presented by DR. HARRY M. ROBINSON JR., Baltimore.

A. J., a 33 year old Negro woman, was first seen by me in November 1947, at which time the eruption on her back was of two months' duration. Numerous new lesions continue to develop despite a fat-free diet.

On examination numerous nodules are seen on her face, chest and back. They vary in color from lemon yellow to a dull brown. Most of them are globular and firm. Over the surface of the lesion there are dilated capillaries, and there is complete absence of scale. The nodules are quite shiny and vary from 1 to 2 cm. in diameter.

Serologic tests for syphilis gave negative reactions. Results of urinalysis were within normal limits. The hemogram was normal. Blood sugar was 97 mg. per 100 cc., and blood cholesterol was 185 mg. per 100 cc. on Nov. 28, 1947, 465 mg. on March 3, 1948, and 282 mg. on May 6, 1948.

Roentgenologic examination of the chest and long bones showed no abnormalities. Roentgenologic examination of the skull showed one small area of increased density in the parietal area which measured approximately 1.5 cm. in diameter. This was persistent in all the films which have been taken and possibly represents an area of rarefaction in the bone.

On microscopic examination the epidermis was observed to be atrophic. The lesion filled most of the cutis. The tumor was made up of mononuclear cells: most were oval; some were arciform, and others were elongated. Most of the nuclei were large and lightly staining with a few prominent nucleoli. No giant cells were seen. In the hematoxylin-and-eosin-stained section there were very few xanthoma cells, but the fat stains showed a definite increase of lipids in small lobules.

DISCUSSION

DR. WILBERT SACHS, New York: Some years ago Dr. Lewis and I described a case of lipid histiocytoma, another name for fibroxanthoma. Now in those cases the lesions looked very much alike. In other words, all the cells were spindle shaped. In this particular case the cells are not so spindle shaped but they are more epithelioid in character and there appear to me to be too many foam cells for a lipid histiocytoma; I wonder whether this disorder may not be some type of xanthoma. We had a case of xanthoma with keloidal changes, and I'd suggest that possibility.

DR. HERMAN BEERMAN, Philadelphia: I believe that this case may represent a more serious type of xanthomatosis than is suggested by the previous discussion. In conjunction with Drs. Blank and Eglick I have recently recorded a case of so-called nevoxanthoendothelioma with ocular involvement. I was gratified to find that Thannhauser in the new edition of his monograph on the so-called lipidoses has indicated that cases of so-called nevoxanthoendothelioma with visceral manifestations should be classed as perhaps a *forme fruste* type of Hand-Schüller-Christian disease. I would suggest, therefore, that a careful study of the eyes and bones be made in this case.

Nevus Unius Lateris. Presented by DR. FRANCIS A. ELLIS and DR. HARRY M. ROBINSON JR., Baltimore.

P. G., a Negro woman aged 38, has had late latent syphilis. In 1939, while under active antisyphilitic therapy, she was hospitalized because of a lichen-planus-like eruption. By May 1944 she manifested an eruption on the right side of the neck and the right ear. The affected area has become larger.

The eruption consists of hypertrophic to slightly verrucous, subacutely inflamed papular lesions. It tends to be somewhat linear and extends from the eyebrow to the nose, posteriorly to the retroauricular area and caudad to the angle of the mandible. The lesions consist of discrete and grouped papules and plaques measuring 0.5 cm. and larger.

Tuberculin tests gave negative reactions. The blood serologic test for syphilis gave negative reactions.

Microscopic examination of the retroauricular area revealed mild parakeratosis. The epithelium showed an even acanthosis with rete pegs that were fairly wide and extended to the granular layer. The infiltrate was fairly loose and consisted of small and large monocytes, a few polymorphonuclear leukocytes and some eosinophils. In the subpapillary layer there were many dilated capillaries and an area of dense infiltrate consisting of numerous lymphocytes and fibroblasts, a moderate number of plasma cells and polymorphonuclear leukocytes. The biopsy specimen was suggestive of psoriasis, except for the dilated capillaries and dense lymphocytic infiltrate in the midcutis.

DISCUSSION

DR. FRANCIS A. ELLIS, Baltimore: We who saw this lesion develop were somewhat confused by the biopsy specimen. The first one looked so much like psoriasis that we thought there was a mistake and took a second specimen. Although the epidermal changes could be those of psoriasis, there is a deeper infiltrate that does not fit the picture for psoriasis.

DR. WALTER F. LEVER, Boston: It would be most unusual for nevus unius lateris to appear late in life. Also, from the histological point of view, nevus unius lateris is unlikely because of the rather pronounced inflammatory infiltrate in the corium. I consider lichen striatus, which tends to come out quite suddenly and disappears after a certain length of time. Also, the possibility of lupus erythematosus should not be entirely dismissed. This diagnosis is suggested especially by the large bald area above the right ear. I suggest that a biopsy be performed in that area.

DR. WILBERT SACHS, New York: I saw nothing in the slides to indicate lupus erythematosus. The lesions on the face certainly are not those of lupus erythematosus. The lesion on the scalp may possibly be lupus erythematosus now. As far as I know there is no characteristic microscopic picture of nevus unius lateris. One may get a picture quite similar to lichen planus, psoriasis or neurodermatitis or even an epithelial nevus. I agree with the diagnosis as presented. If there is a characteristic picture, as Dr. Lever points out, I am not acquainted with it.

Pseudoxanthoma Elasticum in Mother and Daughter. Presented by DR. RAYMOND A. OSBOURN and DR. MATTHEW A. OLIVO, Washington, D. C.

The cases of B. S., a white woman aged 29, and her daughter, S. S., aged 3, are presented. The mother's skin trouble was first noticed when she was at about the age of 5 years. The neck was the only area affected until age 22, when there was involvement of the axillas, groins and cubital fossae. At age 25 the eruption spread to involve the wrists, popliteal fossae and umbilicus. There is no known skin disorder in other members of the family except the patient's child. There is no parental consanguinity.

Distributed symmetrically over the neck, axillas, groin, umbilicus and popliteal fossae are yellow to chamois-colored papules and plaques. The plaques are slightly elevated, 2 to 5 mm. The older lesions are deeper yellow and present a reticulated appearance on the sides of the neck and linear configuration with an interlacing threadlike pattern in the cubital fossae and axillas. Numerous follicular plugs sprinkled over the neck area give the skin a dirty appearance. The skin over the involved areas is loose and easily stretched, and sparsity of hair is noted in the axillas and pubic area.

An ophthalmologic examination by Dr. Thomas A. Egan, Washington, D. C., showed that in the fundus of each eye angioid streaks were present in the retina. These streaks were in the vicinity of the disk, incompletely surrounding it with irregularly radiating lines coming off the central hub like the spokes of a wheel. They were of a deep brownish color situated deep in the retina underlying the vessels and in many instances parallel to the course of these vessels. Both macular areas themselves were free of involvement. Ophthalmologic examination showed an otherwise normal condition.

The hemogram was normal, as were the results of urinalysis. The blood Kahn reaction was negative, and blood chemistry was normal.

On microscopic examination the epidermis showed moderate hyperkeratosis and some flattening of the rete ridges. The papillary layer was essentially normal. In the midcutis were degenerative changes in the elastic tissue, with the fibers swollen, fragmented and clumped.

The history for S. S. is as follows: When the child was 8 months of age her mother noticed that the skin on the neck showed wrinkling. This condition has become more pronounced and the skin more yellowish.

The skin of the neck shows parallel ridges and yellowish folds. There is no follicular plugging, but some pilosebaceous orifices are dilated. In the axillas the only change in the skin consists in accentuated furrows of a light yellow color.

Ophthalmologic examination of S. S., also by Dr. Egan, revealed no abnormality.

DISCUSSION

DR. DAVID BLOOM, New York: A definite diagnosis of pseudoxanthoma elasticum should not be made in this case without a biopsy, for the following reason: the presence of this condition in the mother and child is unusual for pseudoxanthoma elasticum, which is transmitted according to the recessive mode of inheritance. In order that the child inherit this condition it would be necessary that the father be a carrier, a heterozygote. I therefore think that for absolute certainty a biopsy should be performed on a specimen from the lesion in the child.

DR. RAYMOND A. OSBOURN, Washington, D. C.: We were aware of the fact that this disorder is considered predominantly a condition with recessive characteristics. I am sorry that the child could not be shown. The lesions on her neck look very much like those of the mother clinically. However, we are still unable to get a biopsy specimen.

Congenital Ichthyosiform Erythroderma. Presented by Dr. Albert Shapiro, Baltimore.

L. W., a white man aged 45, has had the eruption since birth. It always exacerbated during the winter months. His family history is noncontributory.

There is a generalized erythroderma covered with profuse flaky scales. Many of the patches are telangiectatic, and definite atrophy can be noted, particularly below the waist. Some of the areas are secondarily lichenified. Large hyperkeratotic, verrucous plaques are present on the palms, soles, hands, feet and ankles. Linear fissures can be noted in the midst of these keratotic areas. Numerous closely grouped pinhead-sized keratotic papules are present on the right half of the upper part of the back.

The hemogram was normal. The blood serologic test for syphilis gave a positive reaction with a titer of 8 units. (The patient has no history of having had antisyphilitic therapy.)

Microscopic examination of a specimen from the forearm revealed that the keratin layer was increased and there was definite follicular plugging. The epidermis was rather atrophic even in the areas of plugging. There was some spotty parakeratosis. There was slight edema in some parts of the basal layer. The follicular plugs consisted of concentric rings of the keratin. There was slight edema in the upper part of the cutis, some dilatation of the capillaries and a moderate infiltrate consisting mostly of lymphocytes and fibroblasts.

A specimen from the extensor surface of a finger showed some hyperkeratosis with follicular plugging and also some parakeratosis and crusting. The epidermis showed an area of atrophy with some edema in the basal layer and exocytosis. In the cutis there were evidence of edema and a moderately dense infiltrate which was increased around the hair follicles. The infiltrate consisted principally of lymphocytes, a few fibroblasts and plasma cells.

DISCUSSION

Dr. Walter F. Lever, Boston: I do not agree with the diagnosis as presented. Clinically, there is not enough hyperkeratosis, the flexural surfaces do not show predominant involvement and, above all, the disease is progressive. In practically all cases of congenital ichthyosiform erythroderma the disease is severest in infancy and early childhood and then either becomes stationary or improves. I believe that this patient has poikiloderma atrophicans vasculare. The histological picture as seen in the sections is characteristic of that disorder. There is atrophy of the epidermis with vacuolar degeneration of the basal cell layer and invasion of the epidermis by the inflammatory infiltrate. In some areas the upper part of the corium shows fibrosis.

Dr. Francis A. Ellis, Baltimore: I agree with Dr. Lever that histologically the section is not that of congenital ichthyosiform erythroderma. I noticed today something I have not noticed before, that the man does have infiltrated plaques on his thighs which suggest the early changes that one would see in mycosis fungoides, and Dr. Lever may be correct in his diagnosis. It is interesting that the hairs on the dorsal surfaces of his fingers show some hyperkeratosis, as expected in pityriasis rubra pilaris.

Dr. David Bloom, New York: I also wish to agree with Dr. Lever. I have under observation at the Skin and Cancer Unit several women with poikiloderma vasculare atrophicans who, in addition to the skin eruption, have pronounced hyperkeratosis of the palms and soles.

Dr. Wilbert Sachs, New York: I have never seen a case of poikiloderma so generalized as this one. I saw some hyperkeratosis in this case, and I am not acquainted with hyperkeratosis in combination with poikiloderma. I agree with Dr. Ellis. If this condition were poikiloderma, then it would develop into mycosis fungoides. However, this man has had the lesion all his life, and we have one case that was recently written up by Dr. Baer, a case diagnosed as ichthyosiform erythroderma congenitale which later proved to be a mycotic infection; I would suggest that mycologic study be thoroughly carried out on this patient with that possibility in mind.

Dr. David Bloom, New York: I wish to correct that statement of Dr. Sachs. The patient whose case Dr. Baer described and who was under my observation for some time, acquired a mycologic condition superimposed on a congenital ichthyosiform erythroderma.

Cutaneous and Systemic Sporotrichosis. Presented by Dr. Eugene S. Bereston, Baltimore.

W. B., a 46 year old Negro, first had the appearance of "abscesses" on his back in 1944 after having carried bags of fertilizer on his back. New abscesses appeared and then healed with scar formation and crusting. New abscesses with purulent discharge continued to appear on the back and sides of the chest, and the patient later acquired similar lesions about the shoulder girdle, right flank and the foot. Two years ago infiltrative lesions of the lungs were found, and they were still present one year ago.

There are numerous depressed scars on the chest and back with some crusting in these areas. There is some swelling of the left ankle and a number of sinus openings with purulent discharge present on the left foot and ankle.

Fungus cultures of the purulent discharge as well as from incision of new abscesses have repeatedly grown Sporotrichum schenkii. Intradermal tests with Sporotrichum vaccine gave positive reactions in 48 hours. A blood serologic test for syphilis gave a positive reaction, with a titer of 16 units. Infiltrated areas in the lungs and increased hilar markings were seen on a roentgenogram of the chest.

On microscopic examination polymorphonuclear leukocytes, histiocytes, eosinophils, fibroblasts, lymphocytes and plasma cells as well as occasional giant cells were seen in the subcutaneous tissue. No organisms were demonstrated.

The patient received 24 intravenous oxophenarsine hydrochloride (mapharsen®) injections (0.6 Gm.) and 19 intramuscular bismuth subsalicylate in oil injections (0.2 Gm.) between 1947 and 1949. He has had massive doses of orally administered potassium iodide and intravenously given sodium iodide for many months, aureomycin for six weeks in maximum dosage, desensitization with Sporotrichum vaccine and deep roentgen ray therapy. As old lesions heal new ones have appeared despite the above-mentioned therapy.

DISCUSSION

Dr. Ellwood C. Weise, Bridgeport, Conn.: Sporotrichosis being more or less of a regional disease, I would have been very much interested to learn from the presenter the port from which this ship had sailed before arriving in Baltimore. As I understand it, the patient had been unloading bags of fertilizer, and it would therefore make some difference, because of the nature of this disease, from which port this ship had sailed.

Granuloma Fungoides. Presented by Dr. David P. Roberts and Dr. Israel Zeligman, Baltimore.

DISCUSSION

Dr. Walter F. Lever, Boston: I agree with the diagnosis as presented. It is interesting that the nodular lesion shows such a pure infiltrate of reticulum cells that one is almost inclined to make a diagnosis of reticulum cell lymphoma. I wish particularly to discuss therapy in this patient because she has received only roentgen ray treatment. In recent years we have withheld roentgen ray therapy as long as possible in patients with extensive mycosis fungoides because we realized that after a certain length of time the patient becomes resistant to roentgen ray therapy. We have preferred to use therapeutic agents such as urethan or nitrogen mustard. It is my impression that in this patient it may be very much worth while to administer urethane, 4 to 6 Gm. a day.

Dr. Gibson E. Craig, Montreal, Canada: Dr. Kalz at the Royal Victoria Hospital had a case of granuloma fungoides not long ago in which he used an ointment containing 1 per cent podophyllin. As you know, podophyllin has been used in other conditions where mitotic figures are very prevalent. By the use of this ointment, the characteristic changes in the skin disappeared almost miraculously; the disorder came back again a month or two later, but on reapplication of the podophyllin ointment, it was again relieved. This treatment is not in any way a cure, but it certainly relieves the patient of a great deal of discomfort.

Dr. George M. Lewis, New York: In the management of patients with mycosis fungoides it is advantageous to have available several types of therapy in order to treat the patient who is roentgen ray resistant or fails to respond to treatment with urethane or nitrogen mustard.

I have followed for several years an 86 year old man with mycosis fungoides who had a spectacular remission after the use of antimony potassium tartrate. This drug may be kept in mind for the treatment of selected cases, and occasionally it will be effective in these very resistant types of lymphoma. It is prepared commercially in a 1 per cent solution for intravenous use. The starting dose of 3 or 4 cc. should be gradually increased to 6, 8 or even 10 cc. The injections may be given once or twice weekly. The drug must be injected very slowly, to reduce the likelihood of reaction. There has been some intimation that the drug causes myocardial damage, and I think one has to carry on this therapy with that possibility in mind.

Multiple Benign Cystic Epithelioma. Presented by DR. LAWRENCE M. ZELL (by invitation) and DR. MAURICE SULLIVAN, Baltimore.

C. W., a white man aged 22, had the onset of an asymptomatic eruption at age 8. It has slowly spread to its present extent.

On the nose, nasolabial folds, forehead, preauricular areas and cheeks and to a lesser extent on the postauricular areas, lower part of the face, neck and upper part of the back are numerous small firm tumors measuring 0.3 to 0.6 cm. Some are lobulated and traversed by superficial dilated vessels. Intermingled are milia and comedos.

On microscopic examination there were observed numerous cysts containing keratinous material throughout the cutis. Some of these were quite large and were surrounded by what appeared to be a follicular sheath containing all the layers of the epidermis, which in the larger cysts were attenuated and thinned. In some areas there had been branching off of the basal layer to form irregular shapes similar to those observed in basal cell epithelioma. There was moderate inflammatory reaction, dilatation of the blood vessels and degeneration of the collagenous tissue. One small foreign body granuloma with some giant cells was present.

The condition has been unchanged during the past few years, with a progressive increase in the tumor. Tincture of podophyllin was applied twice a day for 14 days without effect to selected areas of six individual tumors. Roentgen rays, 100 r unfiltered, to a 5 cm. square on the center of forehead, were given weekly for six treatments without effect.

Multiple Benign Cystic Epithelioma. Presented by DR. HARRY M. ROBINSON JR., Baltimore.

DISCUSSION OF PRECEDING TWO CASES

DR. LLOYD W. KETRON, Baltimore: I want to disagree with the diagnosis of the condition of the second patient's ears. The histopathologic picture suggests to me a turban tumor. The masses of cells were surrounded by a row of basal cells, and there were hyalin bodies between them, characteristic of turban tumors.

DR. MAURICE SULLIVAN, Baltimore: The case of the young man was presented because of the extensiveness of the eruption and because of the numerous cysts containing keratinous material. Also, it illustrates a type of cutaneous tumor which is unresponsive to podophyllin therapy. The resin podophyllin will cause the involution of any epitheliomatous tumor cells with which it comes directly into contact. The failure in this case can be attributed to the considerable amount of connective tissue interposed between the epidermis and the strands of basal cells in the cutis. Podophyllin is "stopped" by the connective tissue, and the tumor cells are thus protected from its cytotoxic effect.

In connection with the treatment of cutaneous cancer with podophyllin, in the series which I reported (*Bull. Johns Hopkins Hosp.* **85**:200 [Sept.] 1949) of the 25 cutaneous cancers or epitheliomas, 15 have relapsed so far after having initially undergone complete and rapid involution. Podophyllin therapy is therefore not a suitable method because of the inaccessibility of some epithelioma cells lying below a small amount of connective tissue.

DR. JOSEPH GOODMAN, Boston: In a patient with an eruption quite similar to that of the young man, I have been able to produce considerable improvement in appearance by the very simple method of using trichloroacetic acid. I see no reason for not using that procedure in these patients. So far as I am aware, these lesions do not undergo malignant degeneration. The results were very good with the treatment I described, and also I might add that in the

patient to whom I refer roentgen ray therapy, to certain small areas, was entirely unsuccessful in bringing about any improvement.

DR. HARVEY BLANK, Philadelphia: I'd like to ask Dr. Sullivan whether he has any experience with the use of podophyllin chemically other than by local application, for example, in mycosis fungoides.

DR. MAURICE SULLIVAN, Baltimore: We have not used podophyllin in the treatment of granuloma fungoides, but we have tried it for gout and have found it ineffective. This observation was a disappointment because we had expected a response due to the colchicine-like activity of podophyllin. Inasmuch as podophyllin is 20 times less toxic than colchicine we had hoped that it would relieve gout sufferers.

DR. EUGENE F. TRAUB, New York: In view of the question that has just been brought up, of the possible change to a malignant character in cases of multiple benign cystic epithelioma, I can only state that in the past we have seen numerous examples of this disease with associated basal cell epithelioma. Whether the individual lesions of multiple benign cystic epithelioma terminate as basal cell epithelioma or whether they are simply an associated or coincidental observation I do not know, but certainly the association of the two conditions has been recorded time and again. Therefore, in the second case, if some lesions are turban tumors, a variety of basal cell epithelioma, there is no reason why they could not be associated with multiple benign cystic epithelioma of the ear. To answer one of the previous speakers, I do not believe that the therapy could in any way be responsible for a change to a malignant character, since we see so frequently the association of the two types of lesion whether treatment has been given or not.

Lichen Planopilaris. Presented by LIEUTENANT COLONEL F. H. GRAUER and LIEUTENANT COLONEL C. Z. BERRY, Walter Reed General Hospital, Washington, D. C.

About Oct. 21, 1949, R. W. B., a 38 year old white man, first noticed severe pruritus of the dorsum of the right hand and the collar area of the anterior portion of the chest. About 10 days later a macular, erythematous, slightly scaling eruption appeared on these same areas and rapidly spread to involve most of the body, excluding the palms, soles, groin and mucous membranes. The involvement on the face was less than that on the trunk. A routine blood serologic test for syphilis in November 1949 gave a doubtful-positive reaction, as did a repeat examination one week later. Three further repeat serologic tests, on December 1, 2 and 3, all gave negative reactions, as did cerebrospinal fluid examination at the same time. The patient denies taking any drugs prior to the onset of the eruption. He has had no fever, malaise or gastrointestinal upset. He was in the Pacific Theater during the war and had several bouts of malaria with a prolonged history of quinacrine ingestion through most of 1944 and 1945. He had none after that time until after the onset of the present illness, at which time he took about 30 grains (2 Gm.) in one dose on the advice of a medical officer in Germany. His general health has always been excellent.

On the patient's admission to the hospital there was a generalized macular eruption excluding the palms, soles and groin. The individual lesions were smooth, flat, shiny and dusky pink, and some had a slight fine scale. In many of the lesions, especially over the shoulders, there were small spinelike projections. The lesions were about 3 mm. to 1 cm. in diameter. The scalp was covered with a very thick scale, and all the involved areas were very pruritic. Inguinal, supraclavicular and posterior cervical lymph nodes were all enlarged to a moderate degree. The patient has also had some edema of both ankles, more pronounced on the right, but this has been present for several years.

The blood serologic test gave a negative reaction, and determinations of total protein, albumin-globulin ratio, sedimentation rate and fasting blood sugar were all normal, as was a chest roentgenogram. Repeated complete blood counts and results of urinalysis were also normal. Sternal puncture was reported as showing normal marrow.

A lymph node from the right groin was diagnosed on microscopic examination as a reactive node but negative for lymphoblastoma. A lesion from the back was removed and revealed the following changes: The epidermis showed a moderate amount of hyperkeratosis but without significant thickening of the granular layer. The prickle cell layer was variable in

thickness with some areas of atrophy and others showing very deep pointed rete pegs. The basal cell layer showed pronounced liquefaction degeneration. The inflammatory infiltrate contained both polymorphonuclear and mononuclear leukocytes. It was confined to the upper part of the corium, the papillary bodies and the area around the skin appendages, with a collar around the smaller blood vessels of the corium. In addition to the above-mentioned changes, there were some areas which showed follicular plugging and others with a small amount of parakeratosis. The diagnosis was lichen planopilaris, with reactive hyperplasia of lymph nodes.

The condition has improved very slowly. At first the patient was treated with local symptomatic medication, mostly colloid baths and an emollient, and bismuth and crude liver extract given intramuscularly twice weekly. Suberythema doses of ultraviolet radiation three times weekly also have proved beneficial.

DISCUSSION

DR. DAVID BLOOM, New York: I agree with the diagnosis. It may be pertinent to mention here a case which was presented by the late Dr. Abramowitz in 1941 before the Manhattan Dermatological Society (ARCH DERMAT. AND SYPH. **45**:1182 [June] 1942). It was presented with the diagnosis "folliculitis decalvans associated with lichen spinulosus," and the pathological diagnosis was lichen planopilaris. As there was no lesion typical of lichen planus, the relation of lichen planus was denied by the discussers. This patient returned to my associates and me in 1950 with a typical eruption of lichen planus and was presented before the Manhattan Dermatological Society.

DR. WILBERT SACHS, New York: Some years ago I wrote a paper on lichen planopilaris, and though I should like to make that diagnosis here, I am unable to. I can't differentiate this eruption from those that I have seen of quinacrine dermatitis.

LIEUTENANT COLONEL F. H. GRAUER, Washington, D. C.: When we first saw this patient, we were somewhat at a loss as to what the exact diagnosis was. We thought of three possibilities: first, lichen planus; secondly, quinacrine dermatitis, and, thirdly, possibly parapsoriasis. I was interested to see Dr. Sachs bring up the question of quinacrine dermatitis, because we wondered whether perhaps this man—we knew he might have been sensitized several years ago to the drug—might have acquired some eruption such as pityriasis rosea first. In fact, pityriasis rosea was the initial diagnosis made by a medical officer when the patient was first seen in Germany. Then, on taking the large doses of quinacrine, perhaps the patient had a superimposed quinacrine dermatitis. To further substantiate that impression, perhaps, a biopsy specimen which was examined by Dr. Helwig of the Army Institute of Pathology revealed features both of lichen planus and also, possibly, of lupus erythematosus. However, Dr. Helwig made the statement that the cellular infiltrate was in the mid deeper portion of the cutis, as it is usually seen in ordinary lichen planus, and this observation suggested to him the possibility of quinacrine dermatitis. We examined the patient's finger nails, to see whether there was any evidence of retention of quinacrine, with negative results. Dr. Ellis also examined the slide and said it was compatible with lichen planopilaris. During his illness, the patient has lost considerable quantities of hair in the past few months. When we first saw him, he had a very thick head of hair, and now you can see for yourself that it is thinning rapidly. This development, of course, might be compatible with quinacrine dermatitis or with lichen planopilaris. Taking everything into consideration, we finally decided that this case was probably one of lichen planopilaris.

DR. EDWIN E. BARKSDALE, Washington, D. C.: In my opinion, judging from certain responses observed in the Navy, there certainly is no relation between lichen planus and quinacrine dermatitis. Quinacrine dermatitis, so-called, is a fixed drug eruption and is not related either pathologically or clinically to lichen planus. My associates and I worked this problem out, effectively and conclusively, and we were able to reproduce cases of quinacrine dermatoses by giving quinacrine again; to my mind there is no relation between the so-called quinacrine dermatitis and lichen planus.

DR. EUGENE F. TRAUB, New York: It seems to me that, since this man has had such a very extensive hair loss and since in the past few weeks he felt that the hair had again been growing back rapidly, there may not be any permanent damage to the hair follicles, the question

concerning which seemed to me an important point in settling this diagnosis. This point is particularly important since microscopically one cannot differentiate between lichen planus and lichen-planus-like eruptions seen in quinacrine dermatitis. I am sure that Colonel Grauer considered the diagnosis very carefully, but perhaps, since the case has progressed further, he may feel that the return of the hair would favor the diagnosis of quinacrine dermatitis, as I believe the hair loss in lichen planopilaris is irreversible.

Dr. Robert Stolar, Washington, D. C.: When my associates and I were receiving a few patients from New Guinea with this undiagnosed dermatosis and were attempting to prove that it was quinacrine dermatitis, we gave a few of the patients quinacrine. We gave them daily doses, 1 or 2 tablets. We started off with 2 tablets, and later on we gave them 1. I think I can reasonably say that it took four months before we were convinced that the dermatosis returned after it had once disappeared. Now there may have been some earlier lesions, but this investigation was all a matter of a long time, and a few patients received the drug for about six months before it was well established that the quinacrine reproduced the eruption. If this man has a quinacrine dermatosis from his single large dose of quinacrine, this development does not conform to the situation when we attempted to reproduce the dermatitis in those patients considered to be already sensitized to the drug.

Dr. Wilbert Sachs, New York: As Dr. Traub said, the hair rarely comes back in lichen planopilaris. This patient has some hair return. Another point was that there was no follicular appearance nor was there any scaling around the mouth of the hair follicles on the scalp. Still another point against a diagnosis of lichen planopilaris was the fact that most of the lesions showed clinical atrophy. Microscopically the suggested point was that, though the lesions did look like lichen planus, there was no increase in granular layer, a distinguishing feature between true lichen planus and the lichen-planus-like lesions caused by quinacrine.

Dr. F. J. Eichenlaub, Washington, D. C.: I have been following this case for three or four months, ever since the patient's hospitalization, and frankly I don't know what he has, but I should like to point out that the officers who see him every day assured me that, while the patient is hopefully considering that his hair is regrowing, there has been absolutely no improvement in his hair.

Dermatomyositis (Possible Periarteritis Nodosa, Disseminated Lupus Erythematosus). Presented by Lieutenant Colonel F. H. Grauer, and Major J. Sidney Rice, Walter Reed General Hospital, Washington, D. C.

V. R. K., a 16 year old white girl, had the onset of her disease in March 1947, with scaling and erythema over the knuckles, wrists, elbows, knees and ankles, with some follicular plugging and with periorbital edema. There was diffuse erythema over the cheeks. Multiple joint pains appeared, and dull aching of the muscles, severest in the calves, thighs and arms, occurred with mild exercise, disappearing on rest. The muscles became firmer. Two biopsy specimens of skin of the hands, taken in May 1947, were interpreted as showing a picture compatible with acute disseminated lupus erythematosus. There was a gradual loss of mobility of elbows and knees and anorexia and easy fatigability.

The patient is a tall, rather slightly built young woman who walks with a slow, somewhat rigid gait. There is pronounced facial edema, especially periorbital, and there is scaling of the scalp, upper part of the forehead and periauricular areas. The muscles of the extremities are firmer than normal. Over the elbows and small joints of the hands are dry hyperkeratotic, well circumscribed plaques with follicular plugging. The hands are dry and scaly, with some telangiectasia. There is a moderate flexion deformity of the elbows. The musculature of the arms and shoulder girdle appears somewhat atrophic.

The red blood cell count was 3,700,000, with 71 per cent hemoglobin, and the white blood cell count, 3,300, with a normal differential; there were 350,000 platelets. Results of urinalysis were normal; excretion of urine creatine was 53 mg. in 24 hours, with clearance 95 per cent of normal; porphyrin was not demonstrated; excretion of 17-ketosteroids was 3.53 mg. in 24 hours. In studies of the blood chemistry the following results were obtained: creatinine, 1.1 mg. per 100 cc.; urea nitrogen, 8.4 mg. per 100 cc.; ascorbic acid, 0.163 mg. per 100 cc., and total protein, 6.7 mg. per 100 cc. (albumin-globulin ratio, 1.1). In a test for liver function the retention of sulfobromophthalein was 62 per cent at 2 hours. Roentgenologic examination revealed

soft tissue calcification. Culture from a muscle biopsy specimen produced no growth, aerobic or anaerobic. The sedimentation rate was 38 mm. per hour.

Microscopic examination of the skin of the dorsum of the hand revealed that "Vessels of the dermis showed perivascular round cell infiltration with infiltration and edema of the vessel walls themselves. There was slight edema in the dermis and foci of basal cell obliteration." In a skin and muscle specimen of the anterior aspect of the left thigh there was atrophic epithelium and subepithelial degeneration of collagen. There was diffuse edema of collagen and perivascular infiltration of lymphocytes, plasma cells and mononuclear cells. In many areas blood vessels and subepithelial tissues were thickened and hyalinized, and an occasional area showed an inflammatory focus with necrosis in the vessel walls. The muscle fibers showed acute focal inflammation with many fibers swollen and hyalinized. Peripheral nerves showed a slight inflammation and in some areas degeneration of the myelin sheath. The impression was that the condition was dermatomyositis.

The Army Institute of Pathology made the following comment: "The change in the muscle appeared to be entirely secondary to the changes within the blood vessels. These vascular changes were confined chiefly to arterioles and venules. Many arterioles and venules showed collars of lymphocytic inflammatory cell infiltration accompanied with slight perivascular fixed tissue reaction and in some instances obliteration and destruction of the walls of the vessel with obliteration of the lumen. There were associated changes of degeneration of the skeletal muscle. The present lesion was interpreted as an angiitis of nonspecific type, which might also be considered consistent with periarteritis nodosa."

The patient has received general supportive treatment, peroral iron, physiotherapy (Hubbard tank) and occupational therapy since March 1949. Under this therapy she has shown slow but definite improvement.

DISCUSSION

Dr. Francis A. Ellis, Baltimore: Has there been any attempt to find L. E. cells? This should be an important differential finding. In dermatomyositis one does not find L. E. cells but one can observe some laboratory and systemic changes suggestive of acute lupus erythematosus. One can demonstrate the L.E. cell either from the sternal marrow or by indirect methods.

Dr. Gibson E. Craig, Montreal, Canada: Whether this condition be dermatomyositis or lupus erythematosus really doesn't matter. As far as treatment is concerned, as you know, the various drug companies have been trying to obtain synthetically a drug which would be effective. A drug known as pregnenolone (Δ^5-pregnenolone acetate), which comes in 100 mg. tablets and is given orally with no side effects, has been produced. I would suggest that this patient be given pregnenolone.

Dr. Walter F. Lever, Boston: At the Massachusetts General Hospital several patients with systemic lupus erythematosus were treated with pregnenolone. The use of this drug has already been abandoned because it produced absolutely no beneficial results. On the other hand, testosterone has proved itself of definite value in systemic lupus erythematosus. In order to be effective testosterone must be given in fairly large doses, i. e., from 75 to 100 mg. a day. In one case full benefit was obtained only after the daily dose was raised to 150 mg. Because testosterone causes retention of sodium and water when given in large doses, it is advisable to place the patient on a low sodium diet and to administer ammonium chloride, 6 Gm. a day. Testosterone appears to be a safe drug, even in the large doses suggested, as long as one watches out for edema and stops administration of the drug if edema should develop.

Dr. Jacob H. Swartz, Boston: My experience in the treatment of dermatomyositis has consisted simply in the attempt to correct nitrogen balance. In my experience such large doses as Dr. Lever mentioned are not necessary. Smaller doses are just as effective and much less dangerous. A dose of 25 mg. every other day or three times a week is sufficient. Where there is no disturbance of nitrogen balance testosterone does not help in dermatomyositis.

Lieutenant Colonel F. H. Grauer, Washington, D. C.: This discussion has been very stimulating. This patient first manifested her symptoms at 13 years of age in 1947, and with the appearance of the skin eruption she had symptoms referable to the joints and her muscles tired easily and were painful at the end of the day of activity. We did not see her at that time. She was seen at Walter Reed Hospital and admitted, and at that time we thought she had

disseminated lupus erythematosus. I saw her two years later, and at that time, because of the pronounced contractures at the elbows and knees, the atrophy of the muscles and arms and shoulder girdle, I felt certainly that the muscle changes far outweighed the skin manifestations at that time and favored a diagnosis of dermatomyositits. Furthermore, I felt that the cutaneous manifestations, namely, the periorbital edema and erythema which was much more pronounced last year than it is now, together with lupus-erythematosus-like or poikiloderma-like lesions on the extremities, were compatible with dermatomyositis. With regard to the microscopic observations, a biopsy specimen of the muscles was examined by Dr. Helwig of the Army Institute of Pathology, and he felt that the main changes were in the vessels—in other words, that the changes in the muscles were probably secondary to the vascular changes. Now, as you know, Dr. Hamilton Montgomery feels that in dermatomyositis there is a primary parenchymal degeneration of the muscles and the changes in the muscles are not secondary to the vascular changes, whereas in scleroderma the vascular changes are far more pronounced and any muscular changes are secondary to that. However, not all pathologists are in agreement with this contention, and, while I hesitate to delay the discussion, if any of the pathologists here would care to say a word about that, I would think it would be very interesting. When the patient was admitted to the hospital last year, she was thoroughly studied on the medical service. Most of the laboratory observations were within normal limits.

DR. JACOB M. SCHILDKRAUT, Trenton, N. J.: Mention was made here a few minutes ago of pregnenolone. I had occasion to treat a patient with disseminated lupus with a synthetic preparation, of a higher structural formula than pregnenonlone, called artisone® (21-acetoxy-pregnenolone). The results were the usual ones: the patient died within 10 days.

Epidermolysis Bullosa Hereditaria. Presented by DR. ISRAEL ZELIGMAN and DR. HARRY M. ROBINSON JR., Baltimore.

DISCUSSION

DR. H. HANFORD HOPKINS, Baltimore: I should like to ask whether anyone has seen a case of this disease treated with ACTH, and with what results?

DR. WALTER F. LEVER, Boston: One case of epidermolysis bullosa was treated with ACTH at the Children's Medical Center in Boston. No beneficial results were obtained. Just as a side note, I have treated with ACTH three patients with pemphigus vulgaris. One patient who was in a serious condition when treatment was started died although the skin lesions improved. In the other two patients all lesions cleared under treatment with ACTH and the eruption is being kept in check by repeated short courses of ACTH, consisting of daily doses of from 100 to 200 mg. for four to five days.

DR. MAURICE J. COSTELLO, New York: The discussion which is pending is not germane to the general discussion, but as long as it was brought up, four patients who had been treated with ACTH, all with full remissions, were presented at the Academy the other night by members of the staff of the Presbyterian Medical Center.

Sarcoid or Noncaseating Tuberculosis of the Negro. Presented by DR. FRANCIS A. ELLIS, Baltimore.

Sarcoidosis. Presented by DR. HARRY M. ROBINSON JR., Baltimore.

Sarcoidosis. Presented by DR. HARRY M. ROBINSON JR. and DR. MORRIS M. COHEN, Baltimore.

Sarcoidosis. Presented by DR. LEON GINSBURG, Baltimore.

Sclerodermatous Changes Associated with Chronic Porphyria. Presented by DR. ISRAEL ZELIGMAN, Baltimore.

Juxta-Articular Nodes (Rheumatic Nodules). Presented by DR. HARRY M. ROBINSON SR., Baltimore.

Generalized Telangiectasia Spreading Gradually for Five Years. Presented by DR. LLOYD W. KETRON and DR. ISRAEL ZELIGMAN, Baltimore.

Chronic Discoid Lupus Erythematosus of the Scalp; Nevus of the Tongue. Presented by DR. MARK HOLLANDER and DR. MORRIS M. COHEN, Baltimore.

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USE OF ETHYL CHLORIDE IN MINOR DERMATOLOGIC SURGERY

To the Editor:—Under the title of "Use of Ethyl Chloride in Minor Dermatologic Surgery," E. R. Gross and C. S. Wright published a short report in the ARCHIVES for January, 1951 about the procedure, suggesting that it is something new. When I entered the Clinic of Dermatology of the University of Prague in 1906 this method was then in use. I do not know who first recommended it; however, in his monograph on condyloma acuminatum in Finger's "Handbuch der Geschlechtskrankheiten" (Alfred Hölder, 1910), G. Scherber mentioned *Vereisung mit Aethylchlorid* (freezing with ethyl chloride) as one of the treatments of warts. H. Paschkis also described the removal of warts under anesthesia with ethyl chloride in his "Kosmetik für Aerzte" (Alfred Hölder, 1911). E. Jakobi's "Atlas der Hautkrankheiten," (Berlin-Wien, 1912, Vol. 2, Urban and Schwarzenberg) described the treatment of verrucae vulgares and condylomata acuminata by removal with a sharp spoon under ethyl chloride local anesthesia.

Ethyl chloride belonged to the standard equipment of the Austro-Hungarian Army in 1914-1918; it was in all hospitals and in the front line was used as a local anesthetic in the removal of warts, including condylomata acuminata; incision of furuncles and abscesses, and excochleation of lupus vulgaris and granulations of healing wounds, etc. This procedure was observed by American physicians who took postgraduate work in Europe many years ago. I wonder why it is not mentioned in our textbooks of dermatology.

HUGO HECHT, M.D., Cleveland, Ohio.

News and Comment

GENERAL NEWS

Meeting of the Society for Investigative Dermatology, Inc.—The Society for Investigative Dermatology will hold its annual meeting at the Ritz-Carlton Hotel, Atlantic City, N. J., June 7 to 8, 1951.

ANNOUNCEMENTS

Supplementary Edition of Motion Picture Reviews Now Available.—The Committee on Medical Motion Pictures of the American Medical Association has completed the first supplement to the second revised edition of the booklet entitled "Reviews of Medical Motion Pictures." This supplement contains 86 reviews of medical and health films reviewed in *The Journal of the American Medical Association* from Dec. 31, 1949 to Jan. 1, 1951. Each film has been indexed according to subject matter. The purpose of these reviews is to provide a brief description and an evaluation of motion pictures which are available to the medical profession.

Copies of this supplement are available on request to:

The Committee on Medical Motion Pictures, American Medical Association, 535 North Dearborn Street, Chicago 10, Ill.

CORRECTION

In the article by Drs. Finnerud and Riddell on "Polythionic Acid in the Therapy of Acne Vulgaris and Seborrheic Dermatitis" in the March issue of the ARCHIVES, page 375, the word "not" should precede "tried" in point 3 of the summary, which should read "Dermasulf® did not discolor the hair or scalp of any of the patients for whom it was prescribed, but it was not tried in the cases of patients with white hair because frequently such preparations cause staining of white hair."

Obituaries

SIR ERNEST GRAHAM-LITTLE, M.D., F.R.C.P., M.P.
1867-1950

With the passing of Ernest Graham-Little the British school of dermatology has lost one of its most revered and distinguished members.

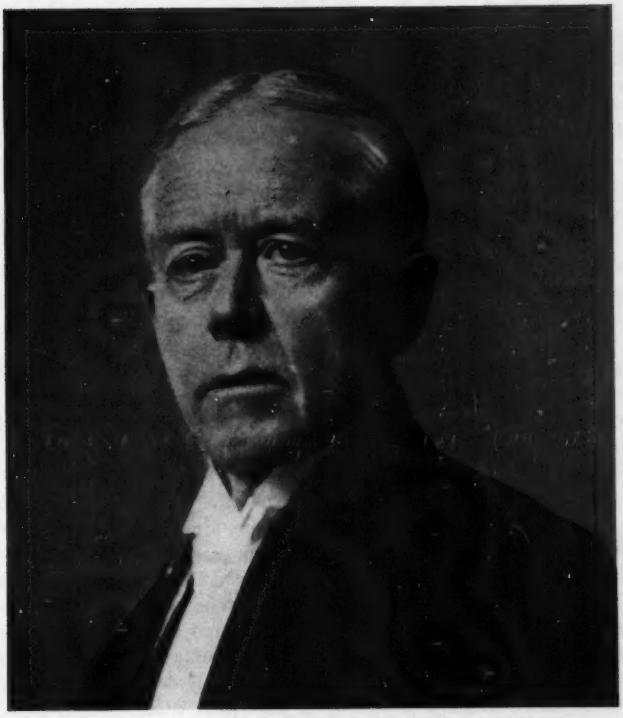
Small in stature but large in intellect, with a remarkable pertinacity of purpose, keenness of observation, indefatigable industry and an ability to write with clarity, Graham-Little made himself a power in the dermatological world and a prominent Member of Parliament.

He came from South Africa, the land of his mother, and received his early education at the Cape University, where he graduated B.A. Coming to London he studied medicine at Guy's and St. George's Hospitals, obtained his degree of M.D. (Lond.) and soon after turned to dermatology.

At first he worked on skin diseases in London at a time when Radcliffe-Crocker, Colcott Fox, Malcolm Morris and J. J. Pringle, that eminent coterie, were the leaders of the British school. Later he proceeded to Paris, to sit at the feet of Besnier and Darier. The teaching of the French masters and a wide knowledge of the French literature influenced not only his subsequent writings but also his whole outlook in dermatology. About that time the histopathology of the skin was beginning to attract attention in Britain, largely owing to the teaching of Hebra in Vienna and Unna in Hamburg, and Little, after settling in London, worked for some time on pathology under my direction in my laboratory at Charing Cross Hospital—incidentally, among his fellow students were the late Howard Morrow of San Francisco and Oliver S. Ormsby of Chicago. Though he was an assiduous student Little's interest in pathology was ephemeral, and he gradually concentrated his attention rather on the clinical and therapeutic aspects of skin diseases.

In 1902 he was appointed physician in charge of the Skin Department at St. Mary's Hospital in succession to Sir Malcolm Morris. There he remained for 30 years, during which period he made a reputation for himself as a diagnostician, therapeutist and a "straightforward and sensible" teacher. He was indefatigable in his attendance at meetings of medical societies and chiefly at those of that old and delightful society, the Dermatological Society of London, of which he was one of the last secretaries before it became incorporated in the Royal Society of Medicine. There he showed innumerable cases, and, in looking over the back numbers of the *British Journal of Dermatology* in which the cases were reported, one finds that he seems to have exhibited a considerably larger number than any of his contemporaries, an activity in which he took a modicum of pride.

His astute powers of clinical observation and his facility in writing led him to contribute to the dermatological literature a series of papers, which were veritable monographs, on subjects in which he was specially interested, such as urticaria pigmentosa, lichen planus, granuloma annulare, tuberculosis cutis and what he designated as "erythematoid benign epithelioma."



SIR ERNEST GRAHAM-LITTLE, M.D., F.R.C.P., M.P.
1867-1950

Though responsible for no textbook he was a prolific writer and was in the habit of contributing yearly to the "Medical Annual" a valuable commentary on the progress of dermatology. Dermatological congresses were a delight to him, and his gift of languages, especially French, rendered him a *persona grata* with his Continental colleagues, who responded by making him an honorary or corresponding member of most of the dermatological societies in Europe. He was an honorary member also of the American Dermatological Association, an honor of which he was justly proud. What with his extensive private practice, his hospital activities and the dermatological societies over which, in due course, he presided, he led an exceptionally active medical life up to about 1930. But there was another side to him which, about that time, changed his whole outlook. As a young man he had shown a strong literary and artistic bias. He was an omnivorous reader with an extensive knowledge of English and French literature, regularly attended activities of social clubs and debating societies and was early attracted by the problem of medical education, economics and politics. These tendencies as they developed gradually overshadowed his interest in dermatology.

As early as 1906 he was elected to the Senate of the University of London; in 1924 he was returned as Member of Parliament for the University, and in 1931 he was knighted. He became so preoccupied with his parliamentary duties that he had little or no time for skin diseases and turned his facile pen to writing letters to the press and articles on subjects of current interest in certain of the more serious monthly journals. He became well known as an ardent controversialist and was apt to be sharp edged and even caustic in debate. He abhorred the so-called Socialism in present-day politics and was a fierce opponent of the National Health Service, which he believed with others to have put the clock back in medicine in Britain for years to come.

But beneath his caustic tongue in debate he had a genial and kindly nature and was given to hospitality and beloved by his friends. He was a great walker and, with his fund of information and sense of humor, a companion with whom going on a walking tour was both a pleasure and an education.

He died after a prolonged illness at the age of 83, leaving a tradition of public service unsurpassed by any of his colleagues. Throughout his married life he was encouraged and ably assisted by his accomplished and gracious wife, especially in the numerous social activities incumbent on his position as a Member of Parliament and in the sad and dark days when they lost their only daughter by drowning and their only son, killed in active service in the last Great War.

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1 Gross, Elmer R., M.D.; Wright, Carroll S., M.D.; Oral Bismuth Therapy in Syphilis and Various Dermatoses—Paper presented at the Pennsylvania Medical Society Meeting, October 8, 1946 at Philadelphia, Pennsylvania.

2 Gross, Elmer R., M.D.; Howles, James K., M.D.; Non-Specific Treatment of Dermatoses and Adjunctive Therapy of Syphilis with Oral Sodium Bismuth Triglycollamate. Read before the Section of Dermatology and Syphilology Meeting of the Centennial Meeting of the A.M.A. at Atlantic City, New Jersey, June 12, 1947.

3 Year Book of Dermatology and Syphilology, 1946, page 31.

4 Sawicky, H. H., M.D.; Bistrimate (sodium bismuth triglycollamate) Administered by Mouth in the Treatment of Chronic Discoid Lupus Erythematosus. The Journal of Investigative Dermatology, vol. 9 #3 September 1947.

5 Howles, James K., M.D.; Treatment of Inflammatory-Dermatoses with Oral Bismuth (sodium bismuth triglycollamate). Southern Medical Journal, vol. 41 #11, pages 1033-1041, November 1948.

6 Pascher, Frances, M.D.; Sawicky, H. H., M.D.; Silverberg, M.G., M.D.; and Emmet, Richard, M.D.; Bistrimate for Lupus Erythematosus, Lichen Planus and other Dermatoses. Journal of Investigative Dermatology, vol. 10, #6, June 1948.

7 Miller, Thomas H., M.D. and Delaney, James R., M.D.; Oral Bismuth therapy in Dermatology. Archives of Dermatology and Syphilology, Vol. 60, August 1949.

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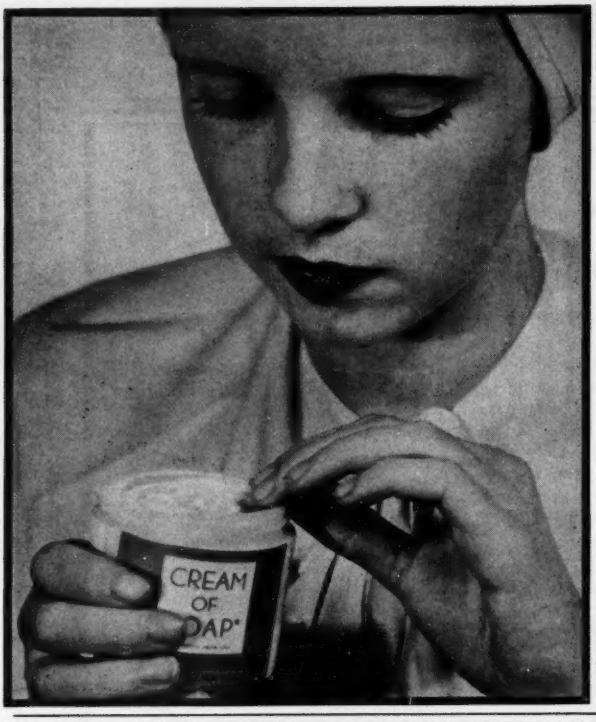

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Archives of Dermatology and Syphilology, February, 1949: 243-245
Abdominal Surgery, Bancroft and Wade, 1947: 804

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Archives of Otolaryngology, March 1947: 294-297
Bulletin of the Johns Hopkins Hospital, Sept. 1948: 225-228
The Eye, Ear, Nose and Throat Monthly, April, 1950: 200-203

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Southern Medical Journal, January, 1951: 42-44

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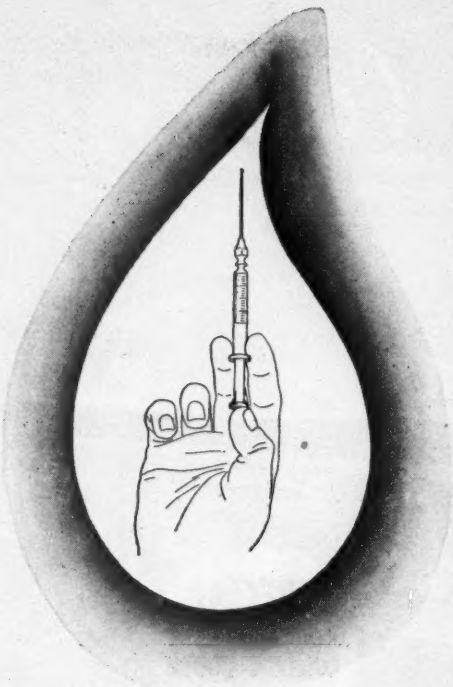

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Extensive experimental studies [6, 9, 16-18] ***proved* CRYSTALLINE DIHYDROSTREPTOMYCIN SULFATE MERCK *less toxic for the vestibular system.***

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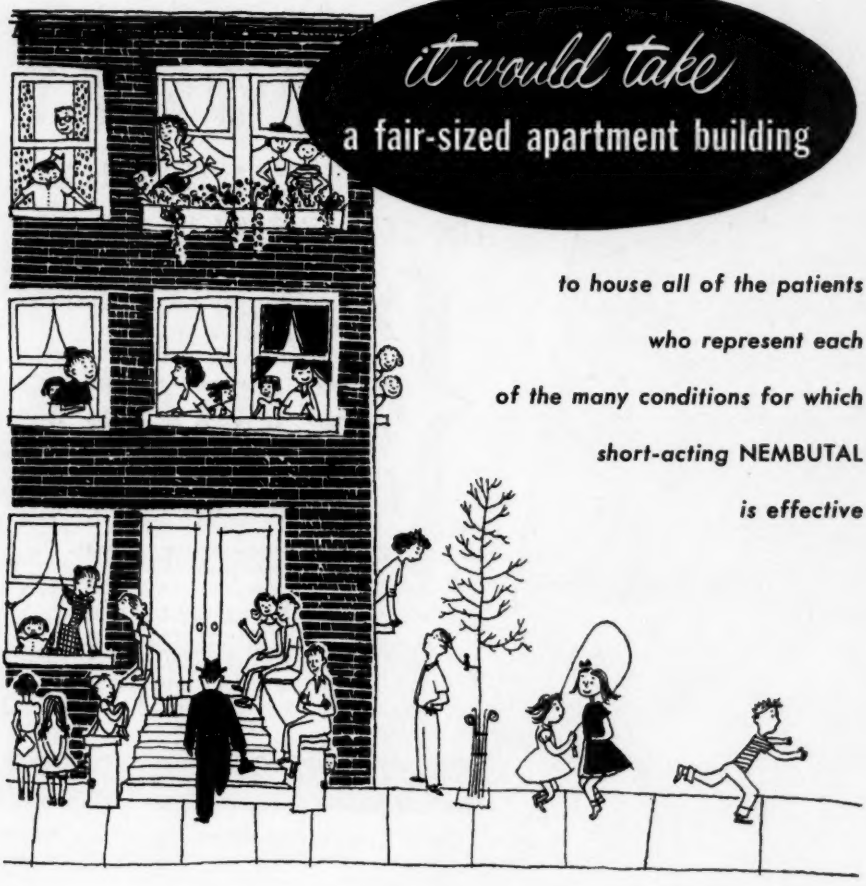

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